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Association of Waist Circumference and Body Mass Index With All-Cause Mortality in CKD: The REGARDS (Reasons for Geographic and Racial Differences in Stroke) Study

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Abstract

Background—Obesity management requires understanding of the mortality risks associated with different adiposity measures.

Study Design—Prospective cohort

Setting and Participants—5,805 adults with BMI ≥ 18.5 and stage 1–4 CKD defined by a spot urine albumin-creatinine ratio ≥ 30 mg/g and/or an estimated glomerular filtration rate < 60 ml/min/1.73 m² enrolled in the REasons for Geographic and Racial Differences in Stroke (REGARDS) study

Predictor—Body mass index (BMI) in kg/m² categorized as 18.5–24.9, 25.0–29.9, 30.0–34.9, 35.0–39.9 and ≥ 40 kg/m² and waist circumference categorized as < 80 , 80–87.9, 88–97.9, 98–107.9, and ≥ 108 cm in women and < 94 , 94–101.9, 102–111.9, 112–121.9, and ≥ 122 cm in men.

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Outcomes—All cause mortality

Measurements—BMI and WC were measured using a standardized protocol during the home visit.

Results—A total of 686 deaths (11.8%) occurred during a median follow-up of 4 years. Compared to the referent BMI category 25–29.9 kg/m², hazard ratios for mortality were 1.27 (95% CI, 0.96–1.69) for BMI < 25 kg/m², and 0.84 (95% CI, 0.62–1.13), 0.81 (0.52–1.26) and 0.95 (95% CI, 0.54–1.65) for BMI categories 30–34.9, 35–39.9 and ≥ 40 kg/m², respectively, after adjustment for covariates including waist circumference. In contrast, after adjustment for covariates including BMI, higher mortality rates were noted for all waist circumference categories compared to the referent (< 80 cm in women and < 94 cm in men) with hazard ratios 1.04 (95% CI, 0.77–1.41) for waist circumference 80–87.9 in women and 94–101.9 in men, 1.29 (95% CI, 0.92–1.81) for waist circumference 88–97.9 in women and 102–111.9 in men, 1.72 (95% CI, 1.12–2.62) for waist circumference 98–107.9 in women and 112–121.9 in men, and 2.09 (95% CI, 1.26–3.46) for waist circumference ≥ 108 in women and ≥ 122 in men.

Limitations—BMI and waist circumference measured at baseline only.

Conclusions—waist circumference should be considered in conjunction with BMI when assessing mortality risk associated with obesity in adults with CKD.

Keywords

Obesity; waist circumference; mortality; chronic kidney disease

Overweight and obesity are associated with excess mortality from diabetes and kidney disease in the U.S. population.¹ Studies which examined the association between body mass index (BMI) and cardiovascular events or mortality in adults with stages 1–4 CKD have found either null or inverse associations, similar to most studies which focused on adults receiving dialysis.^{2–4} However, these investigations did not examine abdominal adiposity and recent data suggest an interaction between BMI and waist circumference on mortality risk among adults receiving dialysis.^{5, 6} Obesity may be measured several ways such as weight per unit of height (body mass index or BMI), waist circumference, waist-to-hip ratio or with direct measures of total body fat. The standard for diagnosing and staging of obesity in the general population remains defined by BMI. However, BMI is a function of both muscle mass and peripheral and abdominal adipose tissue yet the abdominal adipose tissue appears to be the main mediator of cardiovascular risk while peripheral adipose tissue and higher muscle mass appears protective. Waist circumference correlates highly with abdominal adiposity⁷ and may be a better predictor of mortality compared to BMI in adults with CKD who are not receiving dialysis.

Weight reduction may have a role in the management of obese individuals with CKD.^{8, 9} However, interventions to reduce adiposity require an understanding of the mortality risk associated with different weight-related measures. This study examines the association between measures of adiposity, based on BMI and waist circumference, and mortality among adults with CKD prior to the need for dialysis.

Methods

Participants

The REasons for Geographic and Racial Differences in Stroke (REGARDS) study is a population-based cohort of individuals aged 45 years and older and is designed to identify factors that contribute to the excess stroke mortality in the Southeastern United States and among African Americans.^{10, 11} The REGARDS cohort is a national sample of community-

dwelling individuals, 20.9% of whom reside in the coastal plain of North Carolina (NC), South Carolina (SC), and Georgia (GA), 34.5% in the remainder of NC, SC, and GA and the southeastern states of Tennessee, Mississippi, Alabama, Louisiana and Arkansas, and 44.5% in the other 42 contiguous states. There were 30,232 participants recruited into the cohort between January, 2003 and October, 2007.

Baseline information on REGARDS participants were collected by trained staff during a preliminary phone interview followed by an in-home physical examination. The physical exam included blood pressure and anthropomorphic measures and collection of a spot urine specimen and phlebotomy. Participants were instructed to fast 10–12 hours prior to the in-home visit. Figure 1 shows the ordered selection of REGARDS participants included in the analyses. We sequentially excluded 1,298 participants with missing serum creatinine or with an estimated glomerular filtration rate (eGFR) <15 ml/min/1.73m² or who reported treatment for end-stage kidney disease. Further, we excluded 1,106 persons with missing albumin-creatinine ratio measurements, 163 with missing BMI measurements, and 92 with missing waist circumference measurements. Finally, because we were interested in the association between CKD and obesity, we excluded 285 individuals with a BMI <18.5 kg/m², defined by the World Health Organization as underweight.¹² Among these participants, a total of 5805 participants had CKD as defined below.

Kidney Function

A single serum creatinine, calibrated to an international isotope dilution mass spectroscopic (IDMS)-traceable standard, was measured on each participant by colorimetric reflectance spectrophotometry (Ortho Vitros Clinical Chemistry System 950IRC, Johnson & Johnson Clinical Diagnostics, www.orthochemical.com). Estimated glomerular filtration rate (eGFR) was calculated using the CKD Epidemiology Collaboration (CKD-EPI) equation.¹³ Albumin and creatinine were measured in a random spot urine specimen by nephelometry (BN ProSpec Nephelometer, Dade Behring, www.medical.siemens.com) and Modular-P chemistry analyzer (Roche/Hitachi, labsystems.roche.com), respectively. Urine albumin-creatinine ratios (ACR) were calculated in mg/g. Presence of kidney disease was defined according to the NKF's KDOQI CKD stages: stages 1–2 (eGFR ≥ 60 ml/min/1.73 m² and ACR ≥ 30 mg/g) and stages 3–4 (eGFR of 15–59 ml/min/1.73 m²).¹⁴

Obesity measures and mortality

Weight, height and waist circumference (in cm) were measured during the in-home visit following a standardized protocol. BMI was calculated as weight (kg)/height(m²). Waist circumference was measured mid-way between the lowest rib and the iliac crest with the subject standing using a tape measure. At six month intervals following enrollment, vital status was ascertained by telephone contact with participants or with contacts provided at recruitment and by online searches of the Social Security Administrations' Death Master File (ssdi.rootsweb.ancestry.com). The majority of deaths were verified thru online searches and less than 20% were identified thru proxy contact alone.¹⁵ Failed attempts to contact a study participant were followed by phone interviews with alternative contacts which were provided by participants at baseline and updated at each phone contact.

Covariates

We obtained information on physician diagnosis of major co-morbid conditions (coronary artery disease, stroke, cancer, hypertension and diabetes) by self-report during a computer assisted telephone interview. Participants were asked about smoking status, education, family income, and health insurance status. Hypertension was defined as either self-reported use of antihypertensive medications or a SBP ≥ 140 mm Hg or a DBP ≥ 90 mm Hg measured during the home examination, where SBP and DBP were the average of two

measures taken in the seated position. We defined diabetes as a fasting glucose ≥ 126 , or a non-fasting glucose ≥ 200 or current use of either oral hypoglycemic pills or insulin.

Statistical Analysis

Categories of BMI were created based on the World Health Organization classification scheme: 18.5–24.9 kg/m²; 25.0–29.9 kg/m² (referent group), 30.0–34.9 kg/m², 35.0–39.9 kg/m² and ≥ 40.0 kg/m².^{12, 16} Waist circumference categories were created after stratifying participants by sex and were based on the WHO diagnosis of abdominal obesity^{12, 16} with 4 separate categories similar to BMI: < 88 cm in women and < 102 cm in men (referent group), 80–87.9 cm in women and 94–101.9 cm in men, 88–97.9 cm in women and 102–111.9 cm in men, 98–107.9 cm in women and 112–121.9 cm in men, and ≥ 108 cm in women and ≥ 122 cm in men.

Baseline characteristics were compared by BMI and waist circumference categories using ANOVA and χ^2 tests for continuous and categorical variables, respectively and overall P values are reported. Kaplan-Meier curves were constructed to estimate the survival probabilities for all-cause mortality by BMI and waist circumference categories. Cox's Proportional Hazards models were used to estimate the association between measures of obesity and all-cause mortality. The assumptions of the Cox proportional hazards models were examined by plotting the natural log of the cumulative hazard of all cause mortality by the natural log of time. Several proportional hazards models were created to examine the effects of adjustment for covariates. Model 1 adjusted for age, gender and race. Model 2 added the albumin-creatinine ratio (log transformed), eGFR, systolic blood pressure, presence of co-morbid conditions (coronary heart disease, stroke, hypertension and diabetes), smoking status, high density lipoproteins (HDL) and low density lipoproteins (LDL), educational attainment, family income, health insurance status, and access to health care to Model 1. Age, log transformed urine albumin-creatinine ratio, eGFR, systolic blood pressure and HDL and LDL were fitted in the model as continuous variables. To explore potential confounding by body composition, models were also constructed to examine the combined effects of BMI and waist circumference on time to death. Model 3 mutually adjusted for BMI and waist circumference in addition to all of the covariates in Model 2.

We also examined BMI and waist circumference as linear predictors of mortality by fitting both BMI and waist circumference in the model as continuous variables. Interactions between BMI and waist circumference on their respective associations with mortality were examined using Cox proportional hazards models. Effect modification by CKD stage (stages 1–2 and stages 3–4) was explored by placing interaction terms in separate models with BMI or waist circumference as the independent predictor of mortality and adjusting for all covariates. To illustrate the interaction between BMI on the association between waist circumference and all-cause mortality, adjusted hazard ratios (model 2) by waist circumference categories were plotted against BMI as a continuous variable. Due to the strong confounding effects of cigarette smoking and pre-existing disease on the associations between adiposity measures and mortality, analyses were repeated after excluding all current smokers and also after excluding participants who died during the first year of follow-up.

Results

Among the 27,288 REGARDS participants meeting the inclusion criteria, 5,805 (21.7%) were defined as having CKD and included in the analyses. Stage 1–2 CKD was present in 2,922 (50.3%), stage 3–4 in 2,883 (49.7%). Characteristics of participants by BMI and waist circumference categories are shown in Tables 1 and 2, respectively. Participants in the highest BMI category were younger and more likely to be female and African-American compared to the lower BMI categories. In addition, this group was less likely to have a

history of prior stroke, coronary heart disease or cancer or be a current smoker compared to the lower BMI categories. Participants in the highest waist circumference category were also younger and more likely to be female and African-American compared to the lower waist circumference categories. However, the prevalence of prior stroke, coronary heart disease and cancer were fairly similar across the waist circumference categories.

Overall, 686 deaths (11.8%) occurred during a median follow-up of 4.0 years. The mean BMI was lower among participants with CKD who died compared to surviving participants ($29.2 \text{ kg/m}^2 \pm 6.2$ vs. $30.3 \text{ kg/m}^2 \pm 6.5$; $p < 0.05$). In contrast, mean waist circumference was higher among participants with CKD who died compared to individuals with CKD who survived ($101.9 \text{ cm} \pm 15.8$ vs. $99.2 \text{ cm} \pm 15.6$; $p < 0.05$). Figures 2 and 3 show Kaplan-Meier curves demonstrating overall survival by BMI and waist circumference categories, respectively. Overall survival was lowest with BMI $18.5\text{--}24.9 \text{ kg/m}^2$ (Figure 2) while overall survival appeared lowest among waist circumference categories $\geq 98 \text{ cm}$ in women and $\geq 112 \text{ cm}$ in men (Figure 3). Figure 4 shows mortality rates for the five BMI categories by waist circumference categories. The highest mortality rates per 100,000 person-years were noted in BMI categories $< 30 \text{ kg/m}^2$. Within these BMI categories, mortality rates were generally higher among participants in the upper waist circumference categories.

Table 3 shows the adjusted hazard ratios for all-cause mortality by BMI categories. After adjustment for age, sex and race, both the lowest ($18.5\text{--}24.9 \text{ kg/m}^2$) and highest BMI category ($\geq 40 \text{ kg/m}^2$) were associated with a significantly increased hazard rate of mortality compared to the referent category (BMI $25\text{--}29.9 \text{ kg/m}^2$). After further adjustment for all covariates including waist circumference, the lowest BMI category was associated with a higher hazard rate of mortality compared to the referent group (HR, 1.27; 95% CI, 0.96–1.69) but the 95% confidence interval included 1.00. In contrast, all BMI categories with BMI $\geq 30.0 \text{ kg/m}^2$ were associated with reduced hazard rates of mortality compared to the referent group, with all 95% confidence intervals including 1.00.

The association between waist circumference and all-cause mortality was fairly linear and hazard rates of mortality were significantly higher for waist circumference categories $\geq 98 \text{ cm}$ in women and $\geq 112 \text{ cm}$ in men compared to the referent waist circumference category ($< 80 \text{ cm}$ in women and $< 94 \text{ cm}$ in men) after adjustment for age, sex and race (Table 4). Adjustment for all covariates including BMI strengthened these associations with an approximate two-fold increased hazard rate for all-cause mortality noted for waist circumference categories $\geq 108 \text{ cm}$ in women and $\geq 122 \text{ cm}$ in men (HR, 2.09; 95% CI, 1.26–3.46) compared to the referent waist circumference category. Figure 5 shows the association between waist circumference categories and all-cause mortality across the spectrum of BMI. Compared to the referent waist circumference category ($< 80 \text{ cm}$ in women and $< 94 \text{ cm}$ in men), the hazard rate of mortality for the highest waist circumference category ($\geq 108 \text{ cm}$ in women and $\geq 122 \text{ cm}$ in men) increased linearly across the BMI continuum. Hazard ratios for all-cause mortality were lowest for waist circumference categories $80\text{--}107.9 \text{ cm}$ in women and $94\text{--}121.9 \text{ cm}$ in men at the far right end of the BMI distribution compared to the waist circumference referent category.

No interactions were noted by CKD stages on the associations between BMI and all-cause mortality or between waist circumference and all-cause mortality in fully adjusted models. In sensitivity analyses, the exclusion of participants who died during the first year showed very similar results. Furthermore, limiting the analyses to non-smoking participants did not substantially change the associations between BMI and mortality but associations between waist circumference categories and all-cause mortality were strengthened (data not shown). In the full adjusted model which included both BMI and waist circumference as continuous variables, each 1-cm increase in waist circumference was associated with a 2% increased

mortality risk (95% CI, 1.01–1.04), every 1-kg/m² increase in BMI was associated with a 3% decreased mortality risk (95% CI, 0.94–0.99).

Discussion

This study demonstrates substantial differences in the association between BMI and waist circumference and all-cause mortality in adults with CKD. Consistent with previous studies in older adults or adults with co-morbid conditions including stage 5 CKD,^{3, 6, 17, 18} BMI < 25 kg/m² was associated with an increased hazard ratio of mortality compared to BMI 25–29.9 kg/m². We noted that further adjustment for waist circumference led to a reduced risk of mortality among BMI categories ≥ 30 kg/m² compared to a BMI 25–29.9 kg/m². In contrast, a graded and increased mortality risk was noted across increasing waist circumference categories after adjustment for BMI and other covariates.

The current findings are supported by several prior studies which examined the effects of obesity measures on mortality risk with mutual adjustment for BMI and waist circumference in older populations.^{17–19} In the Cardiovascular Health Study (CHS), which followed 5200 men and women aged 65 years and older for over 9 years, BMI was inversely associated with mortality risk after adjustment for waist circumference while the opposite was noted for waist circumference after adjustment for BMI and all other covariates.¹⁷ Mortality risk associated with waist circumference in adults with CKD was examined using pooled data from participants of the Atherosclerosis in Communities (ARIC) and CHS studies with stage 3–4 CKD (1,669 individuals total). Risk of cardiac events (myocardial infarction or cardiovascular death) after an average of 9.3 years of follow-up was 36% (95% CI, 1.02–1.85) higher among individuals with the largest waist-to-hip ratio (≥ 1.02 and 0.96 in men and women, respectively) compared to the group with the lowest waist/hip ratio (≤ 0.95 and 0.87 in men and women, respectively).²⁰ In contrast, no significant association was present between overweight (BMI 25.0–29.9 kg/m²) or obesity (≥30 kg/m²) and cardiac events when compared to BMI 20–24.9 kg/m². Our findings are also consistent with a study by the Calabria Registry of Dialysis and Transplantation Working Group that examined both waist circumference and BMI as predictors of mortality among 537 patients receiving dialysis.⁶ In this study, BMI was inversely associated with reduced all-cause mortality while a linear and direct association was noted between waist circumference and all-cause mortality. After adjustment for BMI and other covariates, every 10 cm increase in waist circumference was associated with a 23% (95% CI, 1.02–1.47) increase in all-cause mortality. In contrast, every 1 kg/m² increase in BMI was associated with an 11% decrease in mortality after adjustment for waist circumference and covariates. Similar findings were noted for cardiovascular mortality.⁶

Clinical guidelines have previously suggested that both BMI and waist circumference should be considered when assessing a patient's risk for adiposity-related disease.²¹ Thus, the findings of this study support previous recommendations for assessment of obesity and its associated cardiovascular risk. Caution should be made when interpreting the observation that a higher BMI is associated with a reduced mortality risk compared to a lower or “ideal” BMI within a population given the absence of information on waist circumference, especially since waist circumference may be elevated among adults within an ideal range of BMI. In the general population, abdominal obesity (a waist circumference > 88 cm in women and > 102 cm in men), is strongly associated with multiple cardiovascular risk factors including hypertension, diabetes, and hyperlipidemia among adults with BMI < 35 kg/m².^{22, 23}

As no significant interaction was noted between BMI or waist circumference and CKD stages, it should be noted that classification of CKD stages 1–2 was based on urine albumin

and creatinine values measured in a single spot urine sample. Approximately 1/3 of adults with microalbuminuria measured in one spot urine sample will not have microalbuminuria in a repeated sample.¹⁴ Thus, misclassification of CKD stages 1–2 is likely. In addition, the follow-up period for this study was less than 5 years and may have been too short to adequately assess mortality risk among a low risk group such as adults with CKD stages 1–2 where mortality risk was approximately half the risk among adults with stages 3–4 CKD. In addition, we did not have information on cause of death and events were limited to all-cause mortality. The strengths of this study include a very large cohort of adults with CKD with a diversity of socioeconomic backgrounds. The REGARDS study was limited to black and white race/ethnicity and additional studies are needed to investigate associations between body composition and mortality in other racial/ethnic groups with CKD. Although waist circumference does correlate highly with abdominal fat in adults with CKD,⁷ another limitation of this study is the lack of direct measures of body composition.

In conclusion, among adults with CKD, BMI by itself may not be a useful measure to determine mortality risks associated with adiposity because it reflects multiple components. Some of these components are directly associated with increased risk of mortality (abdominal adiposity) and other components are not (muscle mass). In contrast, waist circumference reflects abdominal adiposity alone and may be a useful measure to determine mortality risk associated with obesity in adults with CKD, especially when used in conjunction with BMI.

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Figure 1.
Flowchart of REGARDS Participants for Analyses

Figure 2.
Kaplan-Meier Curve for Overall Survival by BMI Categories

Figure 3.
 Kaplan-Meier Curve for Overall Survival by Waist Circumference (WC) Categories

Figure 4.
Distribution of Mortality Rates per 100,000 Person-years by BMI (kg/m²) and Sex Specific (Women/Men) Waist Circumference (WC) Categories

- WC: 80-87.9 cm in women, 94-101.9 for men
- WC: 88-97.9 cm in women, 102-111.9 cm in men
- WC: 98-107.9 cm in women, 112-121.9 cm in men
- WC: ≥ 108 cm in women, ≥ 122 cm in men

Figure 5. Hazard Ratios for All-Cause Mortality by Waist Circumference (WC) Categories Across the Spectrum of BMI with Referent WC Category WC < 80 cm in Women and < 94 cm in Men

Table 1

Baseline Characteristics of the Study Population by BMI Categories

Characteristic	BMI Categories in kg/m ²					
	18.5–24.9	25.0–29.9	30.0–34.9	35.0–39.9	≥ 40	
No. **	1250 (21.5)	2023 (34.8)	1364 (23.5)	714 (12.3)	454 (7.8)	
Age (Years)	72.4 +/- 9.8	70.3 +/- 9.2	76.8 +/- 9.1	65.3 +/- 8.8	63.2 +/- 8.4	
% Male	48.3	55.0	47.6	40.1	28.2 *	
% African-American	34.2	42.0	51.9	56.9	63.7 *	
Waist Circumference						
Men (cm)	88.2 +/- 8.8	97.6 +/- 7.6	107.4 +/- 8.0	119.3 +/- 9.5	131.0 +/- 11.6	
Women (cm)	77.1 +/- 8.4	88.2 +/- 8.7	98.4 +/- 9.4	107.2 +/- 9.8	119.0 +/- 12.7	
% Diabetes	18.8	32.3	45.2	57.3	58.8 *	
% Hypertension	68.7	76.0	82.2	85.7	88.1 *	
% Prior Stroke	12.4	10.8	10.0	11.2	9.5	
% Coronary Disease	31.9	32.5	33.0	32.5	24.7	
% Cancer	18.1	19.7	18.8	13.8	12.2 *	
% Current smoker	21.4	14.2	13.6	11.8	10.9 *	
% Stroke Belt	31.8	33.	34.2	34.6	33.7	
% Stroke Buckle	23.3	18.9	20.2	20.7	24.0	
% Income <\$20,000/year	25.7	24.8	28.2	29.6	40.0 *	
% < High School	15.5	16.8	19.0	18.9	22.5 *	
% No health insurance	4.8	4.6	5.6	8.3	8.8 *	
CKD						
% Stages 1–2	47.2	46.0	52.9	58.5	57.5 *	
% Stages 3–4	52.8	54.0	47.1	41.5	42.5	
SBP (mm Hg)	130.1 +/- 19.9	132.4 +/- 18.6	133.7 +/- 17.9	134.7 +/- 19.2	136.2 +/- 18.2	
eGFR (ml/min/1.73 m ²)	66.1 +/- 23.4	66.4 +/- 24.1	69.2 +/- 24.7	73.4 +/- 26.6	74.0 +/- 28.8	
ACR (mg/g)	3.7 +/- 1.6	3.7 +/- 1.6	3.9 +/- 1.6	4.1 +/- 1.6	4.1 +/- 1.7	

Characteristic	BMI Categories in kg/m ²				
	18.5–24.9	25.0–29.9	30.0–34.9	35.0–39.9	≥ 40
Serum albumin (g/dl)	4.1 +/- 0.4	4.2 +/- 0.3	4.1 +/- 0.4	4.1 +/- 0.3	4.0 +/- 0.3
Hemoglobin (g/dl)	13.3 +/- 1.6	13.4 +/- 1.6	13.3 +/- 1.6	13.2 +/- 1.6	12.8 +/- 1.7
HDL(mg/dl)	55.1 +/- 18.1	48.8 +/- 15.7	47.4 +/- 14.9	46.8 +/- 14.8	47.5 +/- 14.2
LDL (mg/dl)	107.7 +/- 35.1	111.2 +/- 36.5	110.5 +/- 35.6	109.5 +/- 36.4	110.7 +/- 34.6

Note: Continuous data shown as mean +/- standard deviation, categorical data as percentage

* p<0.001; + Ln(ACR)

*** values given in parentheses are percentages

BMI, body mass index; CKD, chronic kidney disease; ACR, albumin-creatinine ratio; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SBP, systolic blood pressure

Conversion factors for units: eGFR in ml/min/1.73 m² to ml/s/1.73 m²; serum albumin and hemoglobin in g/dL to g/L, x10; LDL and HDL in mg/dL to mmol/L, x0.02586.

Table 2
Baseline Characteristics of the Study Population by Sex Specific Waist Circumference Categories

Characteristic	Sex Specific Waist Circumference Categories in cm				
	< 80 (♀); < 94 (♂)	80-87.9(♀); 94-101.9 (♂)	88-97.9 (♀); 102-111.9 (♂)	98-107.9(♀); 112-121.9 (♂)	≥ 108(♀); ≥ 122 (♂)
No. **	1281 (15.8%)	1224 (27.4%)	1386 (23.9%)	997 (17.2%)	917 (15.8%)
Age (Years)	70.8 +/- 10.0	70.3 +/- 9.4	69.4 +/- 9.2	67.7 +/- 9.5	65.4 +/- 8.8
% Male	62.9	58.4	46.8	36.8	26.5 *
% African-American	37.3	40.8	45.2	52.7	60.1 *
BMI (kg/m ²)					
Men	24.7 +/- 2.8	27.9 +/- 2.7	30.6 +/- 3.0	34.1 +/- 3.6	39.3 +/- 6.3
Women	23.4 +/- 2.8	26.6 +/- 3.1	29.7 +/- 3.7	33.6 +/- 4.5	39.7 +/- 6.3
% Diabetes	20.9	27.6	37.4	46.3	61.5 *
% Hypertension	69.3	74.7	79.5	83.3	87.0 *
% Prior Stroke	11.2	10.8	9.5	11.0	12.7
% Coronary Disease	30.7	32.5	32.4	33.6	30.1
% Cancer	17.3	20.8	20.2	16.5	12.9
% Current smoker	16.7	15.0	15.9	14.3	12.3
% Stroke Belt	30.9	33.2	33.4	37.2	33.4
% Stroke Buckle	22.7	18.6	18.8	22.0	21.5
% Income <\$20,000/year	22.7	23.4	27.3	28.4	39.2 *
% < High School	15.1	14.3	19.6	17.2	24.0 *
% No health insurance	5.6	4.2	4.6	6.7	8.1 *
CKD					
%Stages 1-2	50.0	47.6	47.8	52.2	56.6 *
%Stages 3-4	50.0	52.4	52.2	47.8	43.4
SBP (mm Hg)	130.4 +/- 19.0	131.7 +/- 18.4	133.1 +/- 18.6	133.7 +/- 18.7	136.0* +/- 19.3
eGFR (ml/min/1.73 m ²)	67.5 +/- 23.2	67.2 +/- 24.0	66.8 +/- 24.6	69.8 +/- 26.0	72.3* +/- 27.4

Characteristic	Sex Specific Waist Circumference Categories in cm				
	< 80 (♀); < 94 (♂)	80–87.9(♀); 94–101.9 (♂)	88–97.9 (♀); 102–111.9 (♂)	98–107.9(♀); 112–121.9 (♂)	≥ 108(♀); ≥ 122 (♂)
ACR (mg/g)	3.8 +/- 1.58	3.7 +/- 1.56	3.8 +/- 1.62	3.9 +/- 1.62	4.1* +/- 1.62
Serum albumin (g/dl)	4.2 +/- 0.36	4.2 +/- 0.35	4.1 +/- 0.34	4.1 +/- 0.36	4.0* +/- 0.34
Hemoglobin (g/dl)	13.5 +/- 1.6	13.5 +/- 1.6	13.4 +/- 1.6	13.0 +/- 1.6	12.9* +/- 1.6
HDL (mg/dl)	53.9 +/- 17.9	49.1 +/- 16.4	47.8 +/- 15.0	48.3 +/- 14.6	47.5* +/- 15.1
LDL (mg/dl)	107.9 +/- 34.2	111.2 +/- 37.2	112.0 +/- 36.0	109.8 +/- 36.2	109.1 +/- 35.5

Note: Continuous data shown as mean +/- standard deviation, categorical data as percentage

* p<0.001; +Ln(ACR)

** values given in parentheses are percentages

BMI, body mass index; CKD, chronic kidney disease; ACR, albumin-creatinine ratio; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SBP, systolic blood pressure

Conversion factors for units: eGFR in ml/min/1.73 m² to ml/s/1.73 m²; serum albumin and hemoglobin in g/dL to g/L, x10; LDL and HDL in mg/dL to mmol/L, x0.02586.

Table 3

Mortality among Participants with Baseline Stages 1–4 CKD by BMI Categories

		HR(95% CI)		
BMI Categories	Number (%)	Model 1	Model 2	Model 3
18.5–24.9 kg/m ²	1250 (21.5%)	1.25 (1.03–1.51)	1.13 (0.89–1.44)	1.27(0.96–1.69)
25.0–29.9 kg/m ²	2023 (34.8%)	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)
30.0–34.9 kg/m ²	1364 (23.5%)	0.97 (0.78–1.20)	1.07 (0.82–1.38)	0.84 (0.62–1.13)
35.0–39.9 kg/m ²	714 (12.3%)	1.21 (0.93–1.59)	1.25 (0.88–1.77)	0.81 (0.52–1.26)
≥ 40.0 kg/m ²	454 (7.8%)	1.44 (1.03–2.00)	1.58 (1.03–2.43)	0.95 (0.54–1.65)

Model 1 adjusts for age, sex and race.

Model 2 extends Model 1 to include CKD stage and co-morbidities (coronary heart disease, stroke, cancer, hypertension and diabetes), smoking status, educational attainment, household income, health insurance, urine albumin/creatinine ratio, estimated glomerular filtration, systolic blood pressure, HDL and LDL.

Model 3 extends Model 2 to mutually adjust for BMI and waist circumference in all models

Abbreviations: BMI, body mass index; CKD, chronic kidney disease; CI, confidence interval; HR, hazard ratio

Table 4

Mortality among Participants with Baseline Stages 1–4 CKD by Waist Circumference Categories

waist circumference Category	Number (%)	HR (95% CI)		
		Model 1	Model 2	Model 3
< 80 cm (♀); < 94 cm (♂)	914 (15.8%)	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)
80–87.9 cm (♀); 94–101.9 cm (♂)	1591 (27.4%)	1.02 (0.81–1.30)	0.93 (0.71–1.23)	1.04 (0.77–1.41)
88–97.9 cm (♀); 102–111.9 cm (♂)	1386 (23.9%)	1.04 (0.81–1.35)	1.05 (0.80–1.39)	1.29 (0.92–1.81)
98–107.9 cm (♀); 112–121.9 cm (♂)	997 (17.2%)	1.46 (1.12–1.90)	1.27 (0.93–1.74)	1.72 (1.12–2.62)
≥ 108 cm (♀); ≥ 122 cm (♂)	917 (15.8%)	1.58 (1.18–2.10)	1.57 (1.12–2.21)	2.09 (1.26–3.46)

Model 1 adjusts for age, sex and race.

Model 2 extends Model 1 to include CKD stage and co-morbidities (coronary heart disease, stroke, cancer, hypertension and diabetes), smoking status, educational attainment, household income, health insurance, urine albumin/creatinine ratio, estimated glomerular filtration, systolic blood pressure and HDL and LDL.

Model 3 extends Model 2 to mutually adjust for BMI and waist circumference in all models

Abbreviations: BMI, body mass index; CKD, chronic kidney disease; CI, confidence interval; HR, hazard ratio