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Increased body mass index may be associated with greater risk of end-stage renal disease in whites compared to blacks: a nested case–control study

Elvis A. Akwo[1], Kerri L. Cavanaugh[2,3], Talat Alp Ikizler[2,3], William J. Blot[1,4] and Loren Lipworth[1,3*]

Abstract

Background: The relationship between body mass index (BMI) and end-stage renal disease (ESRD) may differ between blacks and whites due to underlying metabolic differences.

Methods: We conducted a nested case–control study of 631 incident ESRD cases and 1,897 matched controls within the Southern Community Cohort Study. Current weight, height, and weight at age 21 were reported at enrollment. Occurrence of ESRD was ascertained by linkage with the United States Renal Data System. With normal BMI (18.5–24.9 kg/m^2) as reference, conditional logistic regression was used to calculate adjusted odds ratios (OR) and corresponding 95 % confidence intervals (CI) for ESRD across other BMI categories by race. In subsequent analysis, BMI at age 21 was modeled using restricted cubic splines with 5 knots. Predicted probabilities of incident ESRD were computed from the multivariable logistic models and plotted against BMI at age 21.

Results: Among blacks, odds of ESRD were significantly increased among those who were overweight (OR: 1.41; 95 % CI: 1.09, 1.83) or obese (OR: 2.56; 95 % CI: 1.88, 3.47) at age 21. Among whites, the association between ESRD and BMI at age 21 was more pronounced, with corresponding ORs of 2.13 (95 % CI: 0.92, 4.93) and 7.46 (95 % CI: 2.90, 19.21; p-interaction 0.05). Only among whites was high BMI at enrollment associated with ESRD risk; OR for BMI ≥ 40 kg/m^2, was 3.31 (95 % CI: 1.08, 10.12). The plot of the predicted probabilities of incident ESRD vs BMI at age 21 showed a monotonic increase in the probability of ESRD after a BMI cutoff ≈ 25Kg/m^2 in both whites and blacks but the slope of the curve for whites appeared greater.

Conclusions: Our results suggest racial differences in the relationship between BMI, both in early adulthood and middle age, and ESRD. These findings warrant further research into understanding the underlying metabolic differences that may explain these differences.

Keywords: Body mass index, End-stage renal disease, Interaction, Blacks, Whites

Background

As the burden of end-stage renal disease (ESRD) in the United States (US) continues to increase [1], it remains important to understand the role of risk factors such as body mass index (BMI), which change during the course of life and which may interact with race to modify ESRD risk. Previous studies have demonstrated strong and significant associations between higher BMI in middle aged adults (and adolescents) and ESRD, which may be explained in part by associations of obesity with inflammation, diabetes and high blood pressure, all of which are risk factors for adverse renal outcomes [2–9]. Given these strong associations, the rising prevalence of early obesity [10] is likely to impact the already substantial health burden associated with ESRD.

A substantially higher incidence of ESRD among blacks than whites has been consistently reported, including

* Correspondence: loren.lipworth@vanderbilt.edu
[1]Department of Medicine, Division of Epidemiology, Vanderbilt University Medical Center, 2525 West End Avenue, Suite 600, Nashville, TN 37203, USA
[3]Vanderbilt Center for Kidney Disease, Vanderbilt University Medical Center, Nashville, TN, USA
Full list of author information is available at the end of the article

among participants of the Southern Community Cohort Study (SCCS), an ongoing prospective cohort study of black and white adults in the southeastern US [11]. The association persists after adjustment for socioeconomic variables and known ESRD risk factors [12–17]. However, to our knowledge, only one study [8], which focused on midlife BMI, has investigated whether there may be a differential relationship between BMI and ESRD in blacks and whites. For any given value of BMI, whites tend to have higher percent body fat than blacks [18], and adiposity has been demonstrated to have different metabolic effects in whites and blacks [19–22].

Therefore, we investigated whether the association between BMI in both early adulthood and midlife and ESRD is stronger among whites compared to blacks, using a nested case–control study within the SCCS.

Methods

Design and study population

Between 2002 and 2009, the SCCS enrolled approximately 86,000 adults (over two-thirds black) aged 40–79 living in 12 southeastern states. Approximately 86 % of participants were recruited at community health centers (CHC), which provide primary health and preventive care services for low-income populations [11, 23], while the remaining 14 % were recruited via mail-based general population sampling. Data on socioeconomic, demographic, lifestyle, and anthropometric characteristics, as well as personal medical history, were ascertained at cohort enrollment via standardized computer-assisted personal interviews for CHC participants, and via self-administered mailed questionnaire for general population participants. Detailed description of SCCS methods has been previously published [11, 23].

The study population for the current nested case–control study was restricted to CHC-enrollees, which ensured that participants were of similar socioeconomic status and had generally equal access to health care at cohort entry regardless of race. Incident ESRD cases were ascertained by linkage of the cohort, using date of birth, Social Security number, and first and last name, with the US Renal Data System (USRDS) from January 1, 2002 to September 1, 2009, the latest date for which data were available. The USRDS registers ESRD cases certified by a physician diagnosis and filed using a medical evidence report form (to the Medicare ESRD program) or when there is other evidence of chronic dialysis or a kidney transplant irrespective of the glomerular filtration rate (GFR) [1, 24]. SCCS participants ($n = 404$) who had a diagnosis of ESRD recorded in the USRDS prior to SCCS enrollment were excluded from our analyses. Three controls were individually matched to each case based on age (±5-year categories), sex and race. Therefore, the study population for the current analysis comprised all 631 ESRD cases identified during the study period and 1,897 matched controls; and with this sample size we had over 82 % power to detect an odds ratio of 1.48.

Assessment of BMI and covariates

The main exposure variable in this study is BMI, defined as weight (kg)/height^2 (m^2), calculated from weight and height self-reported by participants at cohort entry. Participants also reported their weight at age 21. Since BMI at age 21 can indicate long-term exposure to obesity and, given the relatively short follow-up period (median 2.6 years, range: 0–7.2 years) of the cohort, it may be more closely associated than current BMI with an insidious outcome such as ESRD. BMI at age 21was thus considered our primary exposure of interest. We categorized BMI at age 21 using the World Health Organization (WHO) classification as: underweight: <18.5 kg/m^2; normal weight: 18.5–24.9; overweight: 25.0–29.9; obese: ≥ 30.0 [24], and for BMI at cohort entry, further divided the obese category into class I (30.0–34.9), class II (35.0–39.9) and class III (≥40.0).

Statistical analysis

Univariate case–control comparisons were performed using T-tests for continuous variables and chi-square tests for categorical variables; 2-sided p-values were presented. The Pearson's correlation coefficient between BMI at enrollment and BMI at age 21 was computed.

Using normal BMI as the referent, we used conditional logistic regression to estimate odds ratios (OR) and corresponding 95 % CI for ESRD associated with the other BMI categories, overall and stratified by race. We performed the main analyses using BMI at age 21 and, in separate models, considered BMI at enrollment. We investigated race × BMI interactions using a Wald test for the race × continuous BMI interaction term. In addition to the matching variables, covariates included in the main analyses were education (<high school, high school/vocational training/junior college, ≥college), and cigarette smoking (never, former, current). Differences between the crude and adjusted estimates were minimal but we present the adjusted estimates. We did not include history of diabetes or hypertension in our main models given that these may be on the causal pathway between elevated BMI and ESRD. However, in sensitivity analyses, we adjusted additionally for diabetes and hypertension at baseline, in order to examine the magnitude of the association between BMI at age 21 and ESRD independent of these two main intermediates. Also, in order to investigate the influence of short follow-up on the BMI at enrollment-ESRD association, we performed additional sensitivity analyses by successively excluding cases diagnosed within 12, 24 and 36 months after enrollment.

In subsequent analysis, BMI at 21 was modeled using restricted cubic splines with 5 equally spaced knots chosen according to Harrell's percentile distribution: 0.05, 0.275, 0.5, 0.725 and 0.95 corresponding to BMI values of 17.2, 20.7, 22.9, 25.7, 33.8 kg/m^2 respectively [25]. Predicted probabilities of incident ESRD were then computed from the multivariable logistic models and plotted against BMI at 21. Given that potential outliers at the tail ends of the distribution—BMI at 21 < 18.5 kg/m^2 and BMI > 35 kg/m^2—could influence the shape of the curve, we performed sensitivity analyses excluding persons with these values and plotted the curves using splines with knots placed at 20th, 40th, 60th and 80th percentiles of BMI at age 21.

All analyses were performed using STATA (version 12.1, Stata Corp, College Station, Texas, USA) and R version 3.1.1 (R Core Team 2014). For all analyses, p-values < 0.05 were considered statistically significant.

Ethics statement

SCCS participants provided written informed consent, and protocols were approved by the Institutional Review Boards of Vanderbilt University Medical Center and Meharry Medical College.

Results

Among the 2,528 SCCS participants included in this study, 10.4 % were white and 89.6 % were black, and 45.2 % were men. The mean age at enrollment was 53.7 years. The BMI at enrollment and at age 21 were significantly correlated (person correlation coefficient, r = 0.38, $p < 0.0001$), with mean BMI at enrollment (31.2 ± 7.7 kg/m^2) substantially higher than mean BMI at age 21 (23.9 ± 5.5 kg/m^2).

The age and sex distributions of cases and controls were similar given the matched design. Compared with controls, cases were more likely to be in the lowest categories of income and education and were somewhat more likely to be current or former smokers. History of dyslipidemia was reported more frequently by cases than controls, as were diagnoses of diabetes (65.1 % vs 28.5 %) or hypertension (85.7 % vs 65.5 %). Overall, these differences were similar in blacks and whites except for education and BMI at enrollment, for which we found significant differences between cases and controls in blacks but not in whites (Table 1).

Association between BMI at age 21 and ESRD

Odds ratios and 95 % CI for the association between BMI at age 21 and ESRD are presented in Table 2. Overall, compared to persons of normal weight, overweight persons had 44 % higher odds (OR: 1.44; 95 % CI 1.13, 1.85) for ESRD, while obese subjects had an almost 3-fold higher odds (OR: 2.88; 95 % CI 2.16, 3.83) for ESRD.

The results of the stratified analyses (Table 2) show a similar pattern of increasing odds for ESRD with increasing BMI in both blacks and whites. However, the association was substantially stronger in whites. In blacks, the adjusted ORs were 1.41 (95 % CI: 1.09, 1.83) among overweight persons and 2.56 (95 % CI: 1.88, 3.47) among obese individuals. The corresponding ORs in whites were 2.13 (95 % CI: 0.92, 4.93) and 7.46 (95 % CI: 2.90, 19.21). The p-value for interaction in adjusted models revealed a marginally significant effect modification by race of the association between BMI at age 21 and ESRD ($p = 0.05$).

The plot of the predicted probabilities of incident ESRD vs BMI at age 21 showed a monotonic increase in the probability of ESRD after a BMI cutoff ≈ 25 kg/m^2 in both whites and blacks but the slope of the curve for whites appeared greater (Fig. 1). In sensitivity analyses excluding persons with BMI <18.5 kg/m^2 and >35 kg/m^2, the curves for both blacks and whites still showed monotonic increases in the probability of ESRD with increasing BMI at age 21 and the curve for whites was steeper than that of blacks after a BMI of ≈ 27 kg/m^2 (Additional file 1) i.e. the difference in slopes appeared greater in the region were we have the most data: BMI = 18.5–35 kg/m^2.

Association between BMI at enrollment and ESRD

Overall, compared to persons of normal weight, individuals who were overweight or obese at cohort enrollment were not at increased odds of developing ESRD (Table 3). In analyses stratified by race, being overweight (OR: 0.81; 95 % CI: 0.61, 1.07) or obese (OR: 0.80; 95 % CI: 0.61, 1.05) was associated with non-significantly lower odds of ESRD among blacks. On the other hand, whites who were obese had a 2-fold higher odds (OR: 2.17; 95 % CI: 0.94, 4.98) of ESRD, albeit not statistically significant. The p-value for interaction term was = 0.03 in adjusted models, suggesting effect modification by race of the association between BMI at enrollment and ESRD.

In further analyses subdividing the obese groups, among whites, odds of ESRD increased with increasing class of obesity, and those with class III obesity had a significant greater than 3-fold increased odds (OR: 3.31; 95 % CI: 1.08, 10.12) of ESRD. In contrast, among blacks, those with class III obesity did not have significantly increased odds (OR: 1.09; 95 % CI: 0.76, 1.55) of ESRD (Table 3).

Sensitivity analyses

In models additionally adjusted for diabetes and hypertension, the odds of ESRD remained higher in overweight and obese persons, and again the associations were more pronounced among whites, although the strength of the associations was attenuated (Table 4). Compared to normal weight individuals, overweight and obese persons had

Table 1 Baseline characteristics of end-stage renal disease cases and controls in the southern community cohort study

	Overall			Whites			Blacks		
	Cases	Controls	*P*	Cases	Controls	*P*	Cases	Controls	*P*
	N = 631	*N* = 1897		66	198		565	1699	
Age	53.8 (9.0)	53.7 (9.0)	0.75	56.6 (7.8)	56.7 (7.8)	0.96	53.5 (9.1)	53.3 (9.0)	0.73
Age Categories			1.00			0.77			1.0
40–49	243 (38.5)	730 (38.5)		16 (24.2)	47 (23.7)		227 (40.2)	683 (40.2)	
50–59	228 (36.1)	682 (36.0)		30 (45.5)	83 (41.9)		198 (35.0)	599 (35.3)	
60–69	124 (19.7)	375 (19.8)		19 (28.8)	60 (30.3)		105 (18.6)	315 (18.5)	
70–79	36 (5.7)	110 (5.8)		1 (1.5)	8 (4.0)		35 (6.2)	102 (6.0)	
Women	346 (54.8)	1039 (54.8)	0.98	40 (60.6)	120 (60.6)	1.0	306 (54.2)	919 (54.1)	0.98
BMI at age 21 (Kg/m^2)			<0.0001			<0.0001			<0.0001
Underweight	53 (9.0)	214 (11.8)		2 (3.1)	29 (15.0)		51 (9.7)	185 (11.4)	
Normal	291 (49.4)	1101 (60.5)		28 (43.8)	117 (60.6)		263 (50.1)	984 (60.5)	
Overweight	131 (22.2)	357 (19.6)		14 (21.9)	33 (17.1)		117 (22.3)	324 (19.9)	
Obese class I	66 (11.2)	97 (5.3)		11 (17.2)	8 (4.2)		55 (10.5)	89 (5.5)	
Obese class II	26 (4.4)	27 (1.5)		7 (10.9)	4 (2.1)		19 (3.6)	23 (1.4)	
Obese class II	22 (3.8)	23 (1.3)		2 (3.1)	2 (1.0)		20 (3.8)	21 (1.3)	
BMI at enrollment (Kg/m^2)			0.02			0.14			0.03
Underweight	7 (1.1)	14 (0.7)		1 (1.5)	1 (0.5)		6 (1.1)	13 (0.8)	
Normal	141 (22.7)	382 (20.3)		11 (16.9)	47 (24.0)		130 (23.4)	335 (19.9)	
Overweight	167 (26.9)	553 (29.4)		12 (18.5)	56 (28.6)		155 (27.9)	497 (29.5)	
Obese class I	111 (17.9)	431 (22.9)		16 (24.6)	48 (24.5)		95 (17.1)	383 (22.7)	
Obese class II	96 (15.5)	271 (14.4)		13 (20.0)	23 (11.7)		83 (15.0)	248 (14.7)	
Obese class II	98 (15.8)	230 (12.2)		12 (18.5)	21 (10.7)		86 (15.5)	209 (12.4)	
Diabetes	411 (65.1)	539 (28.5)	<0.0001	46 (69.7)	43 (21.7)	<0.0001	365 (64.6)	496 (29.2)	<0.0001
Hypertension	541 (85.7)	1242 (65.5)	<0.0001	52 (78.8)	120 (60.6)	0.007	489 (86.5)	1122(66.1)	<0.0001
High Total Cholesterol	315 (50.0)	615 (35.3)	<0.0001	43 (66.2)	97 (49.2)	0.02	272 (48.1)	568 (33.6)	<0.0001
Education						0.78			0.01
< High school	262 (41.5)	718 (37.9)	0.035	24 (36.4)	72 (36.4)		238 (42.1)	646 (38.0)	
High school/Vocational training/Junior college	336 (53.3)	1027 (54.1)		33 (50.0)	105 (53.0)		303 (53.6)	922 (54.3)	
College degree or higher	33 (5.2)	152 (8.0)		9(13.6)	21 (10.6)		24 (4.3)	131 (7.7)	
Income			<0.0001			0.55			<0.0001
< $15,000	459 (73.7)	1186 (63.1)		48 (72.7)	135 (69.6)		411 (73.8)	1051 (62.4)	
$15,000–24,999	111 (17.8)	425 (22.6)		11 (16.7)	28 (14.4)		100 (18.0)	397 (23.6)	
≥ $25,0000	53 (8.5)	268 (14.3)		7 (10.6)	31 (16.0)		46 (8.3)	237 (14.1)	
Smoking			0.24			0.80			0.14
Never	218 (34.6)	724 (38.2)		21 (31.8)	55 (27.8)		197 (34.9)	669 (39.5)	
Former	160 (25.4)	445 (23.5)		19 (28.8)	63 (31.8)		141 (25.0)	382 (22.5)	
Current	253 (40.1)	724 (38.2)		26 (39.4)	80 (40.4)		227 (40.2)	644 (38.0)	

*P = p-value for univariate comparisons; Data are means (SD) or Frequencies (%)

We used all the data available for each variable to perform the univariate comparisons. We had no missing data for age, race and gender; <1 % missing for BMI at enrollment, diabetes status, hypertension history, income, education and smoking; and 6.7 % missing for BMI at age 21 in cases and 4.1 % in controls

a 16 % (OR: 1.16; 95 % CI: 0.89, 1.52) and 82 % (OR: 1.82; 95 % CI: 1.32, 2.51) higher odds of ESRD, respectively. In stratified models, whites who were overweight or obese had a 21 % (OR: 1.21; 95 % CI: 0.47, 3.17) and almost 3-fold (OR: 2.81; 95 % CI: 0.99, 8.02) higher odds of ERSD, respectively. Among blacks there was an 18 % (OR: 1.18;

Table 2 The association between BMI at age 21 and end-stage renal disease in the southern community cohort study, overall and stratified by race

	Overall				Whites				Blacks			
	Cases	Controls	OR[a]	95 % CI	Cases	Controls	OR[a]	95 % CI	Cases	Controls	OR[a]	95 % CI
	N = 589	*N* = 1819			*N* = 64	*N* = 193			*N* = 525	*N* = 1626		
BMI Category												
Underweight	53	214	0.89	0.63, 1.25	2	29	0.19	0.02, 1.46	51	185	0.99	0.69, 1.41
Normal	291	1101	1.00 (referent)	N/A	28	117	1.00 (referent)	N/A	263	984	1.00 (referent)	N/A
Overweight	131	357	1.44	1.13, 1.85	14	33	2.13	0.92, 4.93	117	324	1.41	1.09, 1.83
Obese	114	147	2.88	2.16, 3.83	20	14	7.46	2.90, 19.21	94	133	2.56	1.88, 3.47

Abbreviations: *BMI* Body Mass Index, *CI* Confidence Interval, *OR* odds ratio, *N/A* not applicable

P value for race × continuous BMI interaction term (test for additivity) in adjusted model = 0.05 (in the unadjusted model, the *P* value = 0.047)

[a]Adjusted for education (<high school, completed high school, vocational training or junior college and ≥ college degree), and smoking history (never, former and current). Age, gender and race were matching factors in the conditional logistic models

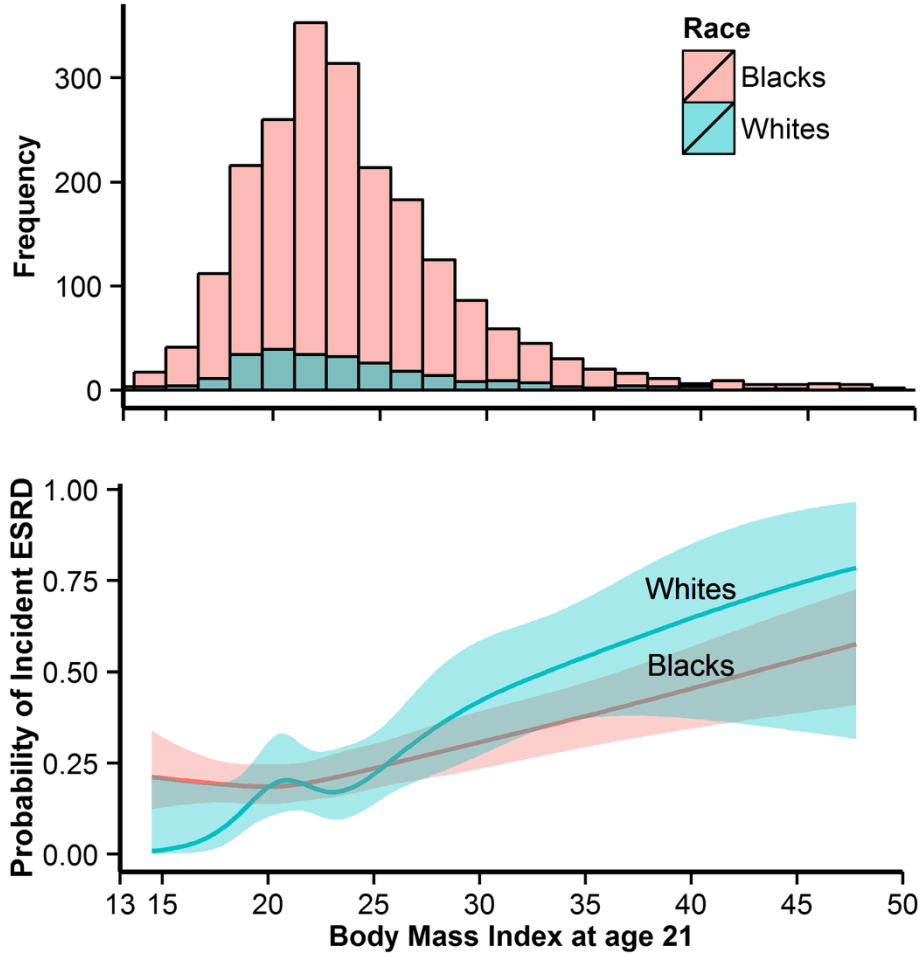

Fig. 1 The predicted probabilities of incident ESRD for whites and blacks, plotted against BMI at age 21. BMI at age 21 was modeled using restricted cubic splines with 5 knots. Predicted probabilities of incident ESRD computed from multivariable logistic models were plotted against BMI at age 21. There is a monotonic increase in the probability of ESRD after a BMI cutoff ≈ 25 kg/m^2 in both whites and blacks but the slope of the curve for whites appears steeper

95 % CI: 0.89, 1.57) and 71 % (OR: 1.71; 95 % CI: 1.22, 2.41) higher odds of ESRD in overweight and obese individuals, respectively (p-value for interaction = 0.29).

In analyses restricted to cases (and their matched controls) with more than 12 months of follow-up, we observed non-significant increased odds for ESRD in whites in the overweight, and class I and II obesity categories (compared to the normal weight), and a significant 4-fold (OR: 3.99; 95 % CI: 1.11, 14.35) increased risk for those in the class III obesity category. In contrast, there was no increased risk among blacks with class III obesity (OR: 1.02; 95 % CI: 0.70, 1.52). In additional analyses restricted to cases with more than 2 or more than 3 years of follow up, the associations with ESRD in the highest BMI categories were more pronounced, but again the point estimates were substantially higher in whites compared to blacks. In particular, in the analyses restricted to those with more than 3 years of follow-up, there was a non-significant 5-fold (OR: 5.04; 95 % CI: 0.32, 79.49) increased odds of ESRD among whites with class III obesity, as compared to a corresponding non-significant 45 % (OR: 1.45; 95 % CI: 0.84, 2.51) increased odds of ESRD among blacks (data not shown).

Discussion

In this case–control study nested within the SCCS cohort of low-income blacks and whites, we found that the association between elevated BMI (both in early adulthood and midlife) and ESRD differed by race. Among both black and whites, being overweight or obese in early adulthood (age 21) was associated with a higher risk of ESRD, but the magnitude of the association was considerably stronger in whites compared to blacks. Being obese in

Table 3 The association between BMI at enrollment and end-stage renal disease in the southern community cohort study, overall and stratified by race

	Overall				Whites				Blacks			
	Cases	Controls	OR[a]	95 % CI	Cases	Controls	OR[a]	95 % CI	Cases	Controls	OR[a]	95 % CI
	N = 620	*N* = 1881			*N* = 65	*N* = 196			*N* = 555	*N* = 1685		
BMI Category												
Underweight	7	14	1.27	0.49, 3.28	1	1	3.54	0.18, 69.17	6	13	1.06	0.39, 2.92
Normal	141	382	1.00	N/A	11	47	1.00 (referent)	N/A	130	335	1.00 (referent)	N/A
Overweight	167	553	0.83	0.64, 1.08	12	56	0.99	0.38, 2.59	155	497	0.81	0.61, 1.07
Obese	305	932	0.89	0.69, 1.14	41	92	2.17	0.94, 4.98	264	840	0.80	0.61, 1.05
Obese I	111	431	0.72	0.53, 0.96	16	48	1.63	0.65, 4.17	95	383	0.65	0.47, 0.88
Obese II	96	271	0.97	0.70, 1.33	13	23	2.62	0.96, 7.12	83	248	0.86	0.61, 1.22
Obese III	98	230	1.21	0.86, 1.69	12	21	3.31	1.08, 10.12	86	209	1.09	0.76, 1.55

Abbreviations: *BMI* Body Mass Index, *CI* Confidence Interval, *OR* odds ratio, *N/A* not applicable

P value for race × continuous BMI interaction term (test for additivity) in adjusted model = 0.03 (in the unadjusted model, the *P* value = 0.02)

[a]Adjusted for education (<high school, completed high school, vocational training or junior college and ≥ college degree)), and smoking history (never, former and current). Age, gender and race were matching factors in the conditional logistic models

Table 4 Sensitivity analysis: the association between BMI at age 21 and end-stage renal disease in the southern community cohort study adjusting for diabetes and hypertension and stratified by race

	Overall				Whites				Black			
	Cases	Controls	OR[a]	95 % CI	Cases	Controls	OR[a]	95 % CI	Cases	Controls	OR[a]	95 % CI
	N = 589	*N* = 1816			*N* = 64	*N* = 193			*N* = 525	*N* = 1623		
BMI Category												
Underweight	53	213	0.92	0.63, 1.33	2	29	0.20	0.02, 1.73	51	184	1.01	0.68, 1.48
Normal	291	1100	1.00 (referent)	N/A	28	117	1.00 (referent)	N/A	263	983	1.00 (referent)	N/A
Overweight	131	356	1.16	0.89, 1.52	14	33	1.21	0.47, 3.17	117	323	1.18	0.89, 1.57
Obese	114	147	1.82	1.32, 2.51	20	14	2.81	0.99, 8.02	94	133	1.71	1.22, 2.41

Abbreviations: *BMI* Body Mass Index, *CI* Confidence Interval, *OR* odds ratio, *N/A* not applicable

[a]Adjusted for education (<high school, completed high school, vocational training or junior college and ≥ college degree), smoking history (never, former and current), diabetes and hypertension. Age, gender and race were matching factors in the conditional logistic models

midlife (mean age at enrollment was 53.7 years) was not associated with increased risk of ESRD among blacks, while among whites a significantly increased risk of ESRD was observed only among those in the highest category of obesity (BMI ≥ 40).

A few studies have previously reported increased risk of ESRD with higher BMI in early adulthood or adolescence. Using data from over 1.2 million adolescents who underwent fitness evaluation for the Israeli military, Vivante and colleagues reported hazard ratios 3.00 (95 % CI: 2.50–3.60) and 6.89 (95 % CI: 5.52–8.59) for ESRD among those who were overweight or obese, respectively, over a 25-year follow-up period [9]. A retrospective Swedish study of 926 cases and 998 controls observed a 3-fold increased odds (OR 3.1, 95 % CI: 2.1–4.8) of chronic renal insufficiency among persons who were overweight at age 20 [5]. Silverwood et al. also reported an association between younger age when first overweight and other overt renal outcomes using data from the UK Medical Research Council National Survey [26]. In particular, those who first became overweight in early adulthood (26 or 36 years) had increased risk of developing stage 3 chronic kidney disease (CKD) in later life [26]. Similarly, children who were overweight in early life (2–20 years) had increased odds of developing CKD compared to those who were never overweight [27]. These prior studies involved predominantly white populations, and our findings for BMI at age 21 among whites are consistent with those results. However, ours is the first study to investigate this association among blacks, who are at highest risk for ESRD, and to specifically test for effect modification by race, with substantially more pronounced associations among whites compared to blacks.

For BMI in middle-age, a number of studies in various populations, primarily Asian and Caucasian, have reported greater than two-fold increased risks of ESRD in overweight or obese individuals [5, 6]. To our knowledge, the study by Hsu and colleagues using data for 320,252 adults (18 % black, 69 % white) and 1,427 ESRD cases from Kaiser Permanente is the only study that investigated potential heterogeneity of the BMI-ESRD relationship in middle-aged blacks and whites. They reported that among blacks, when compared to persons with normal weight, individuals with obesity class II and III had a risk ratio of 5.5 (95 % CI: 4.1–7.5) and 7.2 (95 % CI: 5.0–10.4), respectively; among whites, corresponding risk ratios were 7.2 (95 % CI: 5.2–10.0) and 8.0 (95 % CI: 5.0–12.8) [8]. A major difference between the two studies is the duration of follow up, being relatively short (median ~ 2.6 years) in our investigation compared to that of the Kaiser study (~26 years). Thus, with longer follow-up, it is possible that our results may be more similar, as suggested by our findings of a strong link between ESRD and BMI at age 21 and by our sensitivity analyses hinting at stronger associations of ESRD with middle age BMI among those with longer follow up. Also, differences in socioeconomic status between blacks and whites are likely to be more pronounced in the Kaiser population than in our study population, and thus residual confounding may contribute to the elevated ESRD risk associated with BMI among blacks.

As ESRD and cardiovascular disease (CVD) share risk factors including obesity, one could expect similar racial patterns in BMI-ESRD and BMI-CVD relationships. Previous studies have reported stronger associations between BMI and cardiovascular outcomes in whites compared to blacks [28, 29]. In the SCCS cohort, it has previously been shown that whites with class III obesity had a greater than 2-fold increased risk of cardiovascular death compared to those of normal weight, while in blacks the increase in risk was modest (17–40 %) and non-significant [29]. Similarly, using SCCS data, Lipworth et al. found that in whites the HR for atrial fibrillation was 1.49 (95 % CI: 1.11, 2.01) in obese persons (compared to normal weight persons), while among blacks the corresponding HR was 0.90 (95 % CI: 0.69, 1.16) [30]. Our findings, which suggest a stronger BMI-ESRD association in whites compared to blacks, are thus in line with CVD results in the same cohort.

The underlying reasons for these differential relationships by race remain poorly understood. It is well-established that blacks and whites have different body compositions, whereby on average whites have higher visceral fat and percent body fat than blacks at equivalent BMI [18, 31]. Waist circumference may be a better proxy than BMI for visceral adiposity [32], which is central to the pathophysiology of cardiorenal endpoints. Waist circumference was measured for only about 10 % of SCCS participants, and in the current analysis was available for only 16 ESRD cases and 54 controls. Among whites, waist circumferences was higher (123.3 vs 101.1 cm) in cases ($n = 4$) compared to controls ($n = 13$), while amongst blacks it was similar (103.3 vs 107.7 cm) in cases ($n = 12$) and controls ($n = 41$). While caution is mandatory given the small numbers, these data lend some support to the hypothesis that there may be a differential association between obesity and ESRD by race. Waist circumference was previously shown to be more strongly associated with all-cause mortality in whites compared to blacks [20], raising the possibility that higher adiposity may have less detrimental health effects in blacks compared to whites. The existence of such differential effects and its potential link to differences in metabolic pathways related to inflammation and insulin resistance or gene-environment interactions remains to be explored. Previous studies in the SCCS have also revealed differences in mean levels of BMI-related biomarkers (including adiponectin, leptin, insulin-like growth factor 1, and C-reactive protein) between blacks and whites and in the magnitude of associations of these biomarkers with BMI [19–22],

providing additional evidence that biological mechanisms associated with obesity may differ across racial groups.

The SCCS provides a unique opportunity to examine health disparities for a sizeable number of black participants, who have traditionally been under-represented in most studies focused on cardio-renal outcomes. In addition, both black and white participants had similar income and education levels thereby minimizing confounding by socioeconomic differences; and a high burden of obesity and its comorbidities (diabetes and hypertension). Linkage of the cohort with the USRDS ensured near complete and unbiased ascertainment of ESRD cases. The prospective nature of the nested case–control study design minimized reporting bias on the part of the subjects related to knowing their disease status. Limitations of the study included our reliance on self-reported height and weight for calculation of BMI at enrollment, but a prior validation study for a subset (n = 14,000) of SCCS participants for whom weight and height were abstracted from contemporaneous clinic records showed very high correlation (r >0.95) between self-reported and measured weight and height [29]. Data from the National Health and Nutrition Examination Survey also suggest that BMI based on self-report has good agreement with BMI from measured values [33]. Also, data for weight at age 21 is prone to recall bias which is likely non-differential as data collection was done at baseline before ascertainment of ESRD. Additionally, there may be some variation in BMI throughout early adulthood which a singular value of BMI at age 21 may not completely capture. The limited number of cases among whites curtailed the power of the analyses in this group so we advise some caution in interpreting these results.

Conclusions

In summary, we observed marked racial differences in the relationship between BMI, particularly BMI in early adulthood, and ESRD in a low-income population with a high burden of obesity. This should prompt more research into understanding the underlying metabolic and potential gene-BMI interactions over the lifespan that may explain these differences and which may add to the body of evidence needed to tailor strategies to combat the deleterious effects of obesity.

Additional file

Additional file 1: Sensitivity analysis: predicted probabilities of incident ESRD for whites and blacks, plotted against BMI at age 21 between 18.5 and 35 kg/m^2. BMI at age 21 was modeled using restricted cubic splines with 4 knots and excluding persons with BMI < 18.5 or > 35 kg/m^2. The predicted probabilities of incident ESRD computed from multivariable logistic models were plotted against BMI at age 21. There is a monotonic increase in the probability of ESRD in both whites and blacks but the difference in slopes between the curves appears even greater than in Fig. 1. (PNG 61 kb)

Abbreviations

BMI: Body mass Index; CHC: Community health centers; CKD: Chronic kidney disease; ESRD: End-stage renal disease; SCCS: Southern Community Cohort Study; OR: Odds ratio; USRDS: US Renal Data System; WHO: World Health organization; 95 % CI: 95 % confidence interval.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

EA contributed to the literature review, data analysis, interpretation of the results and writing of the manuscript. LL contributed to the design of the study, acquisition of the data, data analysis, interpretation of the results and writing of the manuscript. KC, AI and WB all contributed to the design of the study, interpretation of the results and writing of the manuscript. All authors read and approved the final manuscript.

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Author details

[1]Department of Medicine, Division of Epidemiology, Vanderbilt University Medical Center, 2525 West End Avenue, Suite 600, Nashville, TN 37203, USA. [2]Department of Medicine, Division of Nephrology, Vanderbilt University Medical Center, Nashville, TN, USA. [3]Vanderbilt Center for Kidney Disease, Vanderbilt University Medical Center, Nashville, TN, USA. [4]International Epidemiology Institute, Rockville, MD, USA.

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