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Variations of Anthropometric Measures of Obesity with Age: The Jackson Heart Study

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Variations of Anthropometric Measures of Obesity with Age: The Jackson Heart Study

Running Title: Obesity and Age

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ABSTRACT

Objective Our objective was to explore anthropometric measures of obesity including body mass index (BMI), waist circumference (WC), waist-to-height ratio (WHtR), and waist-to-hip ratio (WHR) vary with age cross-sectionally and longitudinally among middle and older age African Americans (AAs).

Participants and setting Data for this cross-sectional and longitudinal analysis came from the community-based African-American Jackson Heart Study. We analyzed a total of 3634 JHS participants (mean age: 59.43±12.03; 65% women) who had complete anthropometric measures at Visit 2 and covariate information.

Outcome measures Anthropometric measures of obesity included body mass index (BMI), waist circumference (WC), waist-to-height ratio (WHtR), and waist-to-hip ratio (WHR).

Methods A cross-sectional analysis was conducted using linear regression models to estimate the mean differences of each anthropometric measure across age groups. Changes in anthropometric measure over time (i.e., the effect of aging) within each sex and age group were analyzed using mixed effects models. All regression models were adjusted for covariates.

Results In cross-sectional analysis, we found that age was associated with decreased BMI and WC, but increased WHR in both sexes. In longitudinal analysis, we found that aging was associated with increased BMI, WC, and WHtR among young age groups. The increasing trend with aging tended to diminish or reverse among older age groups. However, WHR tended to increase with aging among all sex and age groups with the highest standardized unit increase per 5-year aging among the four anthropometric measures of obesity examined.

Conclusions Our results show that among middle age AAs, all four anthropometric measures of obesity examined increases with aging. However, among elderly AAs, WHR is the only

anthropometric measures that showed continued increase with aging. WHR may be a better anthropometric measure for monitoring obesity in older AAs.

Key words: age, ageing, anthropometric measures, obesity, body mass index, waist circumference, waist-to-height ratio, waist-to-hip ratio

STRENGTHS AND LIMITATIONS OF THIS STUDY

- The strengths of this study include the large sample size and longitudinal follow-up of a well-characterized cohort of adult AAs, including a substantial proportion of elderly men and women with anthropometric measures of obesity across two visits, and a relatively high retention rate across visits.
- The longitudinal change in anthropometric measures over the life-course were derived from participants from different birth cohorts. While it is reasonable to assume that the longitudinal trend observed in anthropometric measures may be consistent with the biology of aging irrespective of birth cohort, we cannot be certain without longer term follow-up of participants of the same birth cohort.
- The results may not be generalizable to all AAs across the US, as the sample was drawn solely from residents of Jackson, MS.

INTRODUCTION

Ongoing monitoring of trends in obesity is a global health priority due to increased prevalence of obesity worldwide and its associated morbidity and mortality, trans-generational effects, and disproportionate burden in disadvantaged populations[1-4]. Reports of variations in prevalence of obesity by age, sex, and race/ethnicity are helpful for obesity-related risk stratification as the body distribution of adiposity appears to vary by demographic characteristics[5]. However, to date the literature on trends in obesity by demographic characteristics has focused on age- and sex-variations in prevalence of obesity defined by one anthropometric measure only (e.g., BMI, WC, or WHtR)[6 -11], or on comparison of several anthropometric measures of obesity among select population subgroups[12, 13]. From public health and clinical monitoring perspectives, an important knowledge gap emerging from this work on trends in obesity across population subgroups is how anthropometric measures of obesity may vary with age cross-sectionally and longitudinally among middle and older age African Americans (AAs) who experience a disproportionate burden of obesity-related health risks in the US[14].

As AAs are known to have relatively less of their body mass in their trunks and relatively more in their extremities compared to non-Hispanic whites[5], a better understanding of variations in age- and sex-related measures of adiposity among AA may suggest which anthropometric measure(s) may be better for monitoring obesity among elderly AA. In this study, we used data from the Jackson Heart Study (JHS), a community-based longitudinal study of cardiovascular diseases among adult AAs in Jackson, MS, to examine age- and sex-related variations in several anthropometric measures of obesity including BMI, WC, WHtR, and WHR, both cross-sectionally and longitudinally.

METHODS

Data Source

The JHS is the largest single-site, population-based cohort study of cardiovascular diseases in AAs. Participant recruitment for the JHS began in 2000, enrolling 5306 AAs from the tri-county area of Jackson, MS metropolitan area. Participants were examined at baseline (V1 2000-2004) and two additional examinations (V2 2005-2008 and V3 2009-2013). Additional details of the JHS study design, recruitment and data collection have been published previously[15-17]. The JHS was approved by the IRBs of the University of Mississippi Medical Center, Jackson State University, and Tougaloo College. Written informed consent was provided by all participants.

Analytic Sample

Because WHR data were only available at V2 and V3, for comparison purposes, anthropometric measures from V2 were used for the cross-sectional analysis of the variations in anthropometric measures by age. Anthropometric measures from V2 and V3 were used for the longitudinal analysis of changes in anthropometric measures due to aging effect. All participants who returned for V2 were included (N=4205). Participants who had missing values of any of the anthropometric measures of interest at V2 (N=142) or covariates (N=429) (physical activity-4; smoking status-60; education-5; alcohol consumption-21; nutrition-339) were excluded, leaving 3634 participants in the analytic sample.

Anthropometric Measures of Obesity

The anthropometric measures of obesity included BMI, WC, WHtR, and WHR. BMI was calculated as (weight (kg)/height (m)^2)[18]. WHtR was calculated as WC (cm)/height (cm) and WHR was calculated as WC (cm)/hip circumference (cm). Weight was measured to the nearest 0.1 kg and height to the nearest centimeter in light clothing and in stocking feet; WC was measured to the nearest centimeter at the umbilicus; hip circumference was measured to the nearest centimeter at the maximal protrusion. Obesity status (obese/non-obese) was classified based on cut-points recommended by guidelines or reported in the literature for each obesity measure as follows: BMI ≥ 30 (kg/m^2)[19]; WC > 88 cm for women or > 102 cm for men[20, 21]; WHtR ≥ 0.5[22]; WHR ≥ 0.85 for women or ≥ 0.9 for men[23]. For comparison purposes, we computed sex-specific z-scores for each anthropometric measure to put them on the same scale, i.e., in standardized (SD) unit, using the sex-specific means and standard deviations from the analytic sample (all V2 and V3 measurements were pooled to calculate the sex-specific means and standard deviations for each anthropometric measure).

Covariates

Covariates included education, physical activity, smoking status, alcohol consumption, and nutrition collected at V1. Education was based on self-reported years of schooling completed and included 4 categories: less than high school (< 12 years), high school graduate or General Educational Development (GED), some college, and college graduate and above.

For smoking status, physical activity, and nutrition, all were self-reported, we used the cardiovascular health metrics from the American Heart Association (AHA) Life's Simple 7™ to classify participants into three categories: poor, intermediate, or ideal. Smoking status was "poor" if the participant was a current smoker; "intermediate" if the participant had quit smoking less than a year prior to V1; "ideal" if the participant had never smoked or had quit smoking more than a year prior to V1. Physical activity was "poor" if the participant had zero minutes of moderate or vigorous leisure activity per week; "intermediate" if the participant did not have at least 150 minutes of moderate, or at least 75 minutes of vigorous, or at least 150 combined (moderate/vigorous) leisure activity per week; "ideal" if the participant had at least 150 minutes of moderate, or at least 75 minutes of vigorous, or at least 150 minutes of combined moderate/vigorous leisure activity per week. Dietary intake was assessed for all participants using the short Delta Nutrition Intervention Research Initiative (Delta-NIRI) food frequency questionnaire (FFQ) with 158 items[24]. The five dietary components used to compute the AHA score, based on a 2000-kcal diet, were (1) fruits and vegetables, ≥ 4.5 cups/day; (2) non-fried fish, ≥ 2 3.5-ounce servings/week; (3) fiber-rich whole grains, ≥ 3 1-ounce servings/day; (4) sodium, ≤ 1,500 mg/day; and (5) sugar sweetened beverages, < 36 fluid ounces/week (≤ 450 kcal/week). "Ideal" diet was defined by a diet including 4–5 components; "intermediate" diet, 2–3 components; and "poor" diet, 0–1 component[25]. Alcohol consumption was dichotomized (yes/no) per participant's response to the question: "In the past 12 months, have you ever consumed an alcoholic beverage?"

Data Availability Statement

Requests for JHS data require approval of a JHS Manuscript Proposal or Ancillary Study Proposal. To protect the confidentiality and privacy of the JHS participants and their family, a Data and Materials Distribution Agreement (DMDA) is required to obtain data. To submit a request for data, complete a data request form (https://redcap.umc.edu/surveys/?%20s=R48NR37HA8)[26].

Statistical Analysis

Cross-sectional analysis

Age at V2 was grouped into five age groups: < 45, 45-< 55, 55-< 65, 65-< 75 and ≥ 75 years to examine the cross-sectional effect of age on anthropometric measures of obesity. The adjusted means of anthropometric measures (in SD unit) by age group were calculated and compared using linear regression models. All regression models were adjusted for sex, education, physical activity, smoking status, alcohol consumption, and nutrition. To examine whether the effect of age may be modified by sex, the significance of sex*age group interaction term was tested by including the interaction term in the statistical models.

Longitudinal Analysis

The longitudinal effect of age (i.e., the effect of aging) on anthropometric measures of obesity was examined by analyzing the change in anthropometric measures (in SD unit) from V2 to V3 (V3 minus V2 measures) versus follow-up time between V2 and V3 (average 3.3 years, range 1.8 to 6.5 years). Follow-up time was rescaled as 5-year increment so that the regression coefficient reflects a change across 5 years. All analyses were stratified by age group at V2 and sex, and performed using mixed effects models with random intercept (individuals) and random slope (follow-up time). All regression models were adjusted for age, education, physical activity, smoking status, alcohol consumption, and nutrition. The significance of the modifying effect of sex was tested by including a sex*follow-up time interaction term in the statistical models.

All reported *P* values correspond to 2-tailed tests and were significant at the 0.05 level. Analyses were performed using Stata/SE 17.0.

Participant Involvement

Participants who met eligibility requirements were asked to bring their family members for the family study, but they were not directly involved in recruitment, or any other steps in this research process. Participants are sent lay summaries of the results of published manuscripts that derived from the JHS. Lay summaries of study findings are also disseminated to the general community and participants at JHS events[26].

RESULTS

Participant characteristics

Table 1 shows the characteristics of participants in the analytic sample. The mean age of the participants was 59.43 ± 12.03 years old (range 25-97) and about 65% were women. Over 85% of the participants had at least a high school education or GED. Compared to younger participants, older participants were more likely to be women, have less than high school education, have poor physical activity. Older participants were also more likely to have ideal smoking and nutrition status and never consumed alcohol beverages in the last 12 months.

The mean (SD) of anthropometric measures are as follows: weight 90.87 (21.00) kg, height 168.54 (9.40) cm, WC 102.04 (15.74) cm, hip circumference 114.16 (14.44) cm, BMI 32.01 (7.09) kg/m2, WHtR 0.61 (0.10), and WHR 0.89 (0.08). The prevalence of obesity defined by BMI, WC, WHtR and WHR were 55%, 68%, 91%, and 64% respectively. Compared to younger participants, anthropometric measures were generally lower in older participants, except for WHtR and WHR, which were higher in older participants. For WC, the largest WC was observed in the 55-< 65 and the 65-< 75 years groups and the smallest in the ≥ 75 years group.

For obesity, the prevalence of obesity increased with age when defined by WHtR (from 86% in 25-< 45 years group to 94% in 75+ years group) and WHR (from 48% in 25 to <45 years old group to 78% in ≥ 75 years group). While the prevalence of obesity defined by BMI generally decreased with age from 63% in 25-< 45 years group to 41% in ≥ 75 years group.

Cross-sectional analysis

Table 2 shows the results of the cross-sectional analysis of standardized anthropometric measures of obesity by age group from linear regression models adjusting for covariates. For BMI and WC, there was an inverse relationship with age, whereas WHR showed a positive relationship with age. For example, the adjusted mean BMI was 0.80 SD unit lower in the oldest age group than in the youngest age group (β (95% CI) -0.80 (-0.94, -0.66)). In contrast, the

Table 1. Characteristics of Jackson Heart Study Participants included in the Analytic Sample

		Age (years)					
Characteristics	**Total**	**25-<45**	**45-<55**	**55-<65**	**65-<75**	**75+**	**p-value†**
Sample Size	3634	415	884	994	941	400	
Age (years), mean (SD)	59.43 (12.03)	39.44 (4.81)	49.72 (2.86)	59.48 (2.99)	69.02 (2.77)	78.94 (3.51)	<0.001
Sex, n (%)							0.109
Women	2362 (65%)	257 (62%)	557 (63%)	644 (65%)	627 (67%)	277 (69%)	
Men	1272 (35%)	158 (38%)	327 (37%)	350 (35%)	314 (33%)	123 (31%)	
Education, n (%)*							<0.001
Less than high school	552 (15%)	8 (2%)	39 (4%)	94 (9%)	245 (26%)	166 (42%)	
High school graduate/GED	685 (19%)	69 (17%)	135 (15%)	173 (17%)	224 (24%)	84 (21%)	
Attended vocational school, trade school, or college	2397 (66%)	338 (81%)	710 (80%)	727 (73%)	472 (50%)	150 (38%)	
Physical Activity, n (%)*							<0.001
Poor	1718 (47%)	137 (33%)	360 (41%)	460 (46%)	513 (55%)	248 (62%)	
Intermediate	1198 (33%)	166 (40%)	324 (37%)	331 (33%)	276 (29%)	101 (25%)	
Ideal	718 (20%)	112 (27%)	200 (23%)	203 (20%)	152 (16%)	51 (13%)	
Smoking Status, n (%)*							<0.001
Poor	397 (11%)	38 (9%)	111 (13%)	132 (13%)	100 (11%)	16 (4%)	
Intermediate	37 (1%)	3 (1%)	16 (2%)	11 (1%)	6 (1%)	1 (0%)	
Ideal	3200 (88%)	374 (90%)	757 (86%)	851 (86%)	835 (89%)	383 (96%)	
Nutrition, n (%)*							<0.001
Poor	2460 (68%)	339 (82%)	676 (76%)	634 (64%)	575 (61%)	236 (59%)	
Intermediate	1117 (31%)	75 (18%)	205 (23%)	338 (34%)	345 (37%)	154 (39%)	
Ideal	57 (2%)	1 (0%)	3 (0%)	22 (2%)	21 (2%)	10 (3%)	
Alcohol Consumption, n (%)*							<0.001
Yes	1672 (46%)	247 (60%)	524 (59%)	490 (49%)	328 (35%)	83 (21%)	
No	1962 (54%)	168 (40%)	360 (41%)	504 (51%)	613 (65%)	317 (79%)	

		Age (years)					
Characteristics	**Total**	**25-<45**	**45-<55**	**55-<65**	**65-<75**	**75+**	**p-value†**
Anthropometric measures, mean (SD)							
Weight (kg)	90.87 (21.00)	98.22 (26.15)	93.29 (21.97)	92.15 (19.75)	88.17 (18.33)	81.09 (17.01)	<0.001
Height (cm)	168.54 (9.40)	169.80 (9.48)	169.66 (9.24)	169.14 (9.51)	167.61 (8.87)	165.43 (9.68)	<0.001
WC (cm)	102.04 (15.74)	102.64 (18.91)	100.88 (16.03)	103.00 (15.25)	102.55 (15.18)	100.46 (13.57)	0.007
Hip Circumference (cm)	114.16 (14.44)	117.30 (16.48)	114.78 (14.79)	114.78 (14.12)	113.16 (13.73)	110.37 (12.79)	<0.001
BMI (kg/m^2)	32.01 (7.09)	34.11 (9.10)	32.43 (7.31)	32.27 (6.80)	31.42 (6.33)	29.61 (5.66)	<0.001
WHtR	0.61 (0.10)	0.61 (0.11)	0.60 (0.10)	0.61 (0.09)	0.61 (0.09)	0.61 (0.08)	0.001
WHR	0.89 (0.08)	0.87 (0.08)	0.88 (0.08)	0.90 (0.08)	0.91 (0.08)	0.91 (0.07)	<0.001
Obesity, n (%)							
Defined by BMI							<0.001
Yes	2013 (55%)	260 (63%)	502 (57%)	588 (59%)	498 (53%)	165 (41%)	
No	1621 (45%)	155 (37%)	382 (43%)	406 (41%)	443 (47%)	235 (59%)	
Defined by WC							0.005
Yes	2484 (68%)	266 (64%)	572 (65%)	710 (71%)	661 (70%)	275 (69%)	
No	1150 (32%)	149 (36%)	312 (35%)	284 (29%)	280 (30%)	125 (31%)	
Defined by WHtR							<0.001
Yes	3297 (91%)	356 (86%)	775 (88%)	910 (92%)	882 (94%)	374 (94%)	
No	337 (9%)	59 (14%)	109 (12%)	84 (8%)	59 (6%)	26 (7%)	
Defined by WHR							<0.001
Yes	2336 (64%)	201 (48%)	480 (54%)	664 (67%)	678 (72%)	313 (78%)	
No	1298 (36%)	214 (52%)	404 (46%)	330 (33%)	263 (28%)	87 (22%)	

*denotes data collected at V1 were used. All other characteristics were based on data collected at V2.

†One-way analysis of variance (ANOVA) was used for comparison of means of continuous variables; chi-square test was used for comparison of proportions of categorical variables.

SD=standard deviation; GED=General Educational Development; CVD=cardiovascular disease; BMI=body mass index; WC=waist circumference; WHtR=waist-to-height ratio; WHR=waist-to-hip ratio.

Table 2. Cross-sectional Analysis of Standardized Anthropometric Measures at V2 by Age Group

	Age (years)					
Anthropometric Measures	**25-<45 (Ref)** β (95% CI)*	**45-<55** β (95% CI)	**55-<65** β (95% CI)	**65-<75** β (95% CI)	**75+** β (95% CI)	**p-value for trend**
BMI	0	-0.25(-0.37,-0.14)	-0.31(-0.42,-0.20)	-0.48(-0.60,-0.36)	-0.80(-0.94,-0.66)	<.0001
WC	0	-0.12(-0.24,-0.00)	-0.01(-0.12,0.11)	-0.09(-0.21,0.03)	-0.27(-0.42,-0.13)	0.018
WHtR	0	-0.12(-0.24,-0.01)	-0.01(-0.12,0.11)	-0.05(-0.17,0.07)	-0.18(-0.32,-0.03)	0.325
WHR	0	0.08(-0.03,0.20)	0.35(0.23,0.46)	0.43(0.31,0.55)	0.48(0.33,0.62)	<.0001

*β coefficient and 95% confidence interval (CI) from linear regression models, adjusting for sex, education, physical activity, smoking status, alcohol consumption, and nutrition.

BMI=body mass index; WC=waist circumference; WHtR=waist-to-height ratio; WHR=waist-to-hip ratio; CI: Confidence Interval; Ref: reference.

adjusted mean WHR was close to half SD unit higher in the oldest age group than in the youngest age group (β (95% CI) 0.48 (0.33, 0.62)). The tests for trend for BMI, WC and WHR were statistically significant ($p < .05$). No statistically significant sex*age interactions were observed (Supplemental Table 1).

Longitudinal analysis

Figure 1 depicts the anthropometric data for longitudinal analysis by sex and age group (< 45, 45-< 55, 55-< 65, 65-< 75, and ≥ 75 years at V2). The mean anthropometric measures of obesity at V2 and V3 were calculated and plotted against the mean age at the respective visits. As shown in Figure 1, the mean BMI and WHtR were higher in women than in men, while the mean WC and WHR were lower in women than in men across time and in all age groups.

Figure 2 shows the results of changes in standardized anthropometric measures of obesity per every 5 years increase in age (aging) from mixed effects models adjusting for covariates, by sex and age group. A positive coefficient (i.e., on the right side of the vertical reference line at ‘0’) indicates an increasing trend with aging and a negative coefficient indicates a decreasing trend with aging. As shown in Figure 2, aging was associated with increased BMI, WC, and WHtR among younger age groups, but the increasing trend tended to be diminished or reversed among older age groups. For example, for BMI, aging was associated with a (marginally) significant increase in BMI in age groups 25-< 45 and 45-< 55 years in both sexes but the trend reversed in age groups 65 years or older in both sexes (Figure 1a). On the other hand, WHR tended to increase with aging across all sex and age groups, although the magnitude of the increasing trend generally decreased in older age groups. Additionally, WHR had the highest SD unit increase with aging among the four anthropometric measures of obesity examined. For instance, among men 45 years and younger, the mean WHR increased by 0.74 (95% CI 0.52, 0.97) SD unit with each 5-year of aging, while the mean BMI, WC, and WHtR increased only by 0.14 (0.05, 0.23), 0.28 (0.16, 0.40), and 0.30 (0.17, 0.42) SD unit, respectively. Statistically significant sex*age interactions were observed in the analysis for WHR among 25-< 45 years group and WC among 45-< 55 years group (Supplemental Table 2) although they are in the same direction, but different magnitudes of the increasing trend among different sexes (Figure 2).

DISCUSSION

In this study of a large sample of adult AA men and women in Jackson, MS, we found that in cross-sectional analyses, compared to the younger age group, the older age group had a lower mean BMI, WC, and WHtR, but a higher mean WHR. In longitudinal analyses, the effect of aging on the changes in BMI, WC and WHtR was similar; with the mean values increasing with aging only among younger groups. In contrast, the mean WHR increased with aging across all age groups.

The observation that BMI, WC and WHtR decreased with aging while WHR increased with aging in the older age group suggests that loss of lean muscle mass or change in the distribution of fat and lean mass with age may play an important role in disease risks associated with obesity in older adults. This may also partially explain why older adults considered to be overweight based on BMI have a lower mortality rate than those with lower BMI (the "obesity paradox")[27]. In a prospective cohort study among male health professionals in the US, a significant positive monotonic association between predicted fat mass and all-cause mortality, and a U-shaped association between predicted lean body mass and all-cause mortality were found, suggesting that the "obesity paradox" may be largely caused by low lean body mass, instead of low-fat mass, in the lower BMI range[28]. In another prospective cohort study of older

British men, it was found that sarcopenia and central adiposity were associated with higher all-cause mortality[29]. In our own analyses in the JHS, we found the relationships between BMI, WC, WHtR and overall mortality to be J-shaped whereas there was a monotonic increasing relationship between WHR and overall mortality, suggesting once corrected for gluteal muscle mass, lower BMI or central adiposity does not afford greater mortality risks[30].

These findings with WHR fit well with the postulated biological changes in old age, including redistribution of adiposity from limbs to visceral with concomitant loss of lean muscle mass, as approximated by waist circumference (central adiposity) and hip circumferences (gluteal muscle), respectively[23]. Therefore, WHR has been reported to be a better predictor of obesity-related risk among older adults than BMI and WC[31, 32].

The strengths of this study include the large sample size and longitudinal follow-up of a well-characterized cohort of adult AAs, including a substantial proportion of elderly men and women with anthropometric measures of obesity across two visits, and a relatively high retention rate (86%) across visits. However, the study has several limitations. First, the longitudinal change in anthropometric measures over the life-course were derived from participants from different birth cohorts. While it is reasonable to assume that the longitudinal trend observed in anthropometric measures may be consistent with the biology of aging irrespective of birth cohort, we cannot be certain without longer term follow-up of participants of the same birth cohort. Furthermore, the results may not be generalizable to all AAs across the US, as the sample was drawn solely from residents of Jackson, MS.

CONCLUSION

Our results show that among middle age AAs, all four anthropometric measures of obesity examined (BMI, WC, WHtR, and WHR) increases with aging. However, among elderly AAs, WHR is the only anthropometric measures that showed continued increase with aging. Our findings suggest that WHR, a measure that captures both central adiposity and body composition, may be an important anthropometric measure to collect to monitor obesity and obesity-related health risks among older African Americans. These findings should be verified in other ethnically diverse populations.

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DISCLAIMER

The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the National Heart, Lung, and Blood Institute; the National Institute for Minority Health and Health Disparities; the National Institutes of Health; or the U.S. Department of Health and Human Services.

AUTHORS' CONTRIBUTIONS

YG–analysis and interpretation of data, drafting and final approval of the manuscript; YM–statistical expertise, helped conduct the literature review, critical review and final approval of the manuscript; RAB– critical review and final approval of the manuscript; AGB– critical review and final approval of the manuscript; AC–conception and design of study, critical review and final approval of manuscript. All authors have read and approved the manuscript.

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Department of Health (HHSN268201800015I) and the University of Mississippi Medical Center (HHSN268201800010I, HHSN268201800011I and HHSN268201800012I).

AVAILABILITY OF DATA AND MATERIALS

As a National Heart, Lung, and Blood Institute (NHLBI)-funded study, the JHS follows the NHLBI's policy for data sharing, which includes depositing the data into the NHLBI's Biologic Specimen and Data Repository Information Coordinating Center (BioLINCC) to make it publicly available to other investigators. The link to the JHS dataset: https://biolincc.nhlbi.nih.gov/studies/jhs/. Download directions are provided on the website. NHLBI further requires the JHS to maintain the accuracy of this dataset, so the JHS Coordinating Center sends modifications to BioLINCC for incorporation as appropriate. Privacy and access settings are controlled by BioLINCC, and the investigators have no influence on these settings.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study was approved by the Institutional Review Board of the University of Mississippi Medical Center (UMMC IRB Tracking Number: 1998-6004; DHHS FWA: 00003630 0000043; IORG: 00000061; IRB Registration: 00005033) and participants provided written informed consent. The JHS is an observational cohort study. No experiments were performed in the study.

PATIENT CONSENT FOR PUBLICATION

Not applicable.

COMPETING INTERESTS

None.

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Legend/caption for Figures

Figure 1's title: Figure 1(a)-(d). Mean anthropometric measures values at Visit 2 to Visit 3 by age-group and sex.

Figure 1's brief explanation: Each line shows the changes of mean anthropometric measure from Visit 2 to Visit 3 for each age group stratified by sex.

yrs=years.

Figure 2's title: Figure 2(a)-(d). Longitudinal analyses of changes of standardized anthropometric measures per 5-year aging by sex and age group.

Figure 2's brief explanation: Mixed effects models with random intercept and random slope were used to test aging effect. Models were adjusted for covariates including age, education, physical activity, smoking status, alcohol consumption, and nutrition.

M=male; F=female; yrs=years; CI=Confidence Interval.

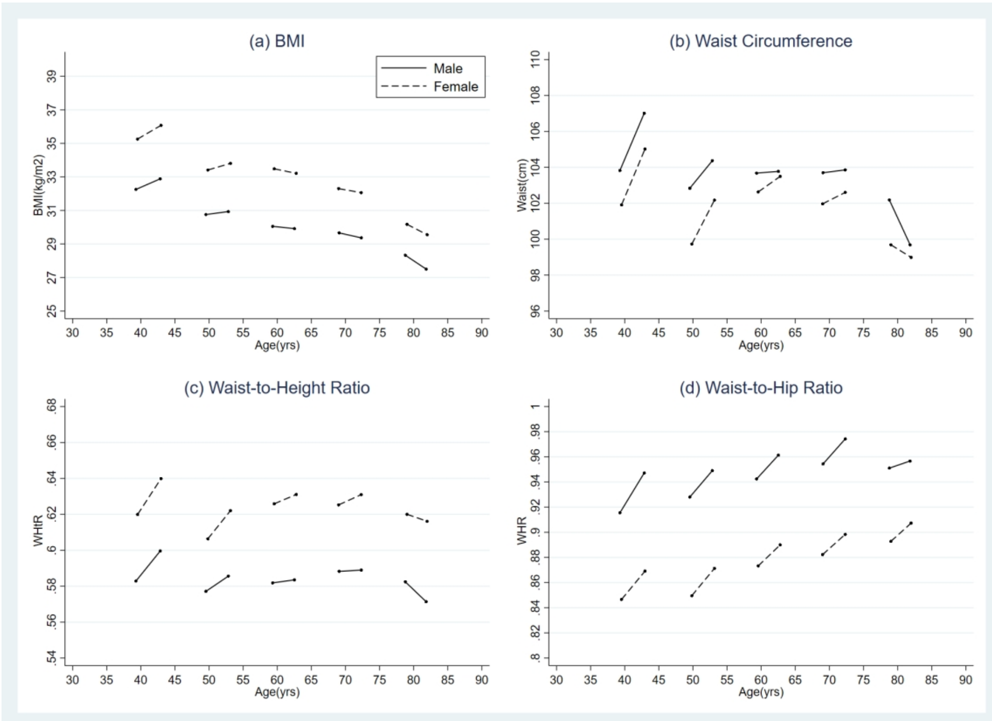

Figure 1(a)-(d). Mean anthropometric measures values at Visit 2 to Visit 3 by age-group and sex. Each line shows the changes of mean anthropometric measure from Visit 2 to Visit 3 for each age group stratified by sex.
yrs=years.

512x372mm (96 x 96 DPI)

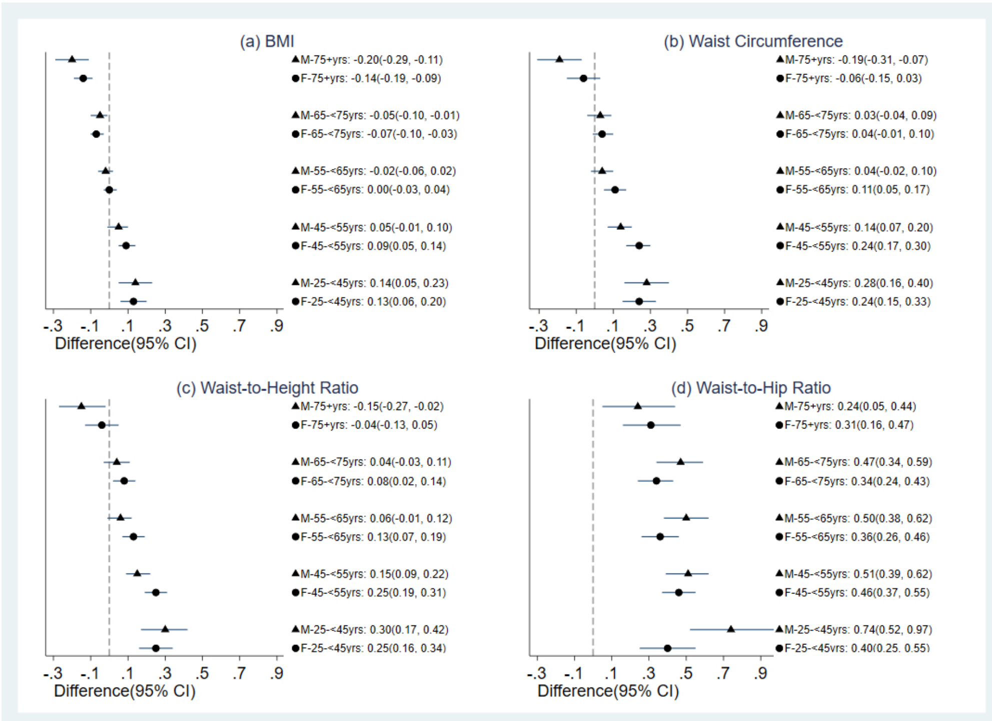

Figure 2(a)-(d). Longitudinal analyses of changes of standardized anthropometric measures per 5-year aging by sex and age group.
Mixed effects models with random intercept and random slope were used to test aging effect. Models were adjusted for covariates including age, education, physical activity, smoking status, alcohol consumption, and nutrition.
M=male; F=female; yrs=years; CI=Confidence Interval.

190x138mm (144 x 144 DPI)

Supplemental Table 1. P-values for effect modification by sex on the associations between obesity measures and age group in cross-sectionally analysis.

Anthropometric Measures	P-value for effect modification by sex
BMI	0.917
WC	0.869
WHtR	0.815
WHR	0.691

The sex*age group interaction term was included in linear regression models adjusting for sex, education, physical activity, smoking status, alcohol consumption, and nutrition.
BMI=body mass index; WC=waist circumference; WHtR=waist-to-height ratio; WHR=waist-to-hip ratio.

Supplemental Table 2. P-values for effect modification by sex on the associations between obesity measures and ageing in each age group in longitudinal analysis.

Anthropometric Measures	25-<45 yrs. age group	45-<55 yrs. age group	55-<65 yrs. age group	65-<75 yrs. age group	75+ yrs. age group
BMI	0.929	0.160	0.475	0.726	0.281
WC	0.657	0.050	0.157	0.792	0.100
WHtR	0.604	0.051	0.139	0.418	0.187
WHR	0.007	0.534	0.082	0.119	0.602

The sex*follow-up time interaction term was included in Mixed effects models with random intercept and random slope were used to test aging effect. Models were adjusted for covariates including education, physical activity, smoking status, alcohol consumption, and nutrition.
BMI=body mass index; WC=waist circumference; WHtR=waist-to-height ratio; WHR=waist-to-hip ratio; yrs.= years.

STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*

Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1-2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2-3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any pre-specified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	5
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	n/a
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5-7
Bias	9	Describe any efforts to address potential sources of bias	n/a
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6-7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7-8
		(*b*) Describe any methods used to examine subgroups and interactions	8
		(*c*) Explain how missing data were addressed	n/a
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed	n/a

		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	n/a
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	5
		(b) Give reasons for non-participation at each stage	n/a
		(c) Consider use of a flow diagram	n/a
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9
		(b) Indicate number of participants with missing data for each variable of interest	n/a
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	n/a
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	n/a
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	9
		Cross-sectional study—Report numbers of outcome events or summary measures	9
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9, 13, 14
		(*b*) Report category boundaries when continuous variables were categorized	n/a
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	13, 14
Discussion			
Key results	18	Summarise key results with reference to study objectives	14
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	15
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14-15
Generalisability	21	Discuss the generalisability (external validity) of the study results	15
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	16-17

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Variations of Anthropometric Measures of Obesity with Age: The Jackson Heart Study

Running Title: Obesity and Age

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ABSTRACT

Objective To explore how anthropometric measures of obesity vary with age among African American (AA) adults.

Participants and setting 3634 AA adults participated in the Jackson Heart Study (Jackson, MS) from 2004 to 2013. .

Outcome measures Body mass index (BMI), waist circumference (WC), waist-to-height ratio (WHtR), and waist-to-hip ratio (WHR).

Methods Linear regression models were used to estimate the mean differences in anthropometric measures cross-sectionally by age group. Longitudinal changes in anthropometric measures over time (*i.e.*, the aging effect) within each sex and age group were analyzed using mixed effects models. All regression models were adjusted for education and lifestyle factors.

Results In cross-sectional analysis, older age was associated with lower BMI, WC, and WHtR, but higher WHR in both sexes. Compared with 25-<44 years age group, the mean (95% CI) BMI, WC, and WHtR was 0.80 (0.66, 0.94), 0.27 (0.13, 0.42), and 0.18 (0.03, 0.32) standardized (SD) unit lower, while WHR was 0.48 (0.33, 0.62) SD unit higher in the 75+ years age group. In longitudinal analysis, aging was associated with increased BMI, WC, and WHtR, among younger age groups but not in older age groups. However, WHR tended to increase with aging across all age groups in both sexes. Among men 75+ years old, the mean change (95% CI) in BMI, WC, and WHtR for every 5 years increase in age, was -0.20 (-0.29, -0.11), -0.19 (-0.31, -0.07), -0.15 (-0.27, -0.02) SD unit, respectively, while it was 0.24 (0.05, 0.44) SD unit for WHR.

Conclusions Among middle-aged AA adults, all four anthropometric measures of obesity examined increased with aging. However, among elderly AA adults, only WHR showed

continued increase with aging. WHR may be a better anthropometric measure for monitoring obesity in older AA adults.

Key words: age, aging, anthropometric measures, obesity, body mass index, waist circumference, waist-to-height ratio, waist-to-hip ratio

STRENGTHS AND LIMITATIONS OF THIS STUDY

- The strengths of this study include the large sample size and longitudinal follow-up of a well-characterized cohort of adult AAs, including a substantial proportion of elderly men and women with anthropometric measures of obesity across two visits, and a relatively high retention rate across visits.
- The longitudinal change in anthropometric measures over the life-course were derived from participants from different birth cohorts. While it is reasonable to assume that the longitudinal trend observed in anthropometric measures may be consistent with the biology of aging irrespective of birth cohort, we cannot be certain without longer term follow-up of participants of the same birth cohort.
- The anthropometric measures from V2 and V3 were used for the analysis, while the covariates including education, physical activity, smoking status, alcohol consumption, and nutritional intake collected at V1 were used for the analysis since they were not collected at V2.
- The results of this study may not be generalizable to all AA adults across the US, as the sample was drawn solely from residents of Jackson, MS.

INTRODUCTION

Ongoing monitoring of trends in obesity is a global health priority due to increased prevalence of obesity worldwide and its associated morbidity and mortality, trans-generational effects, and disproportionate burden in disadvantaged populations [1-4]. Reports of variations in prevalence of obesity by age, sex, and race/ethnicity are helpful for obesity-related risk stratification as the body distribution of adiposity appears to vary by demographic characteristics [5]. However, to date, the literature on trends in obesity by demographic characteristics has focused on age- and sex-variations in prevalence of obesity defined by one anthropometric measure only (e.g., BMI, WC, or WHtR) [6 -11], or on comparisons of several anthropometric measures of obesity among select population subgroups [12, 13]. From public health and clinical monitoring perspectives, an important knowledge gap emerging from this work on trends in obesity across population subgroups is how anthropometric measures of obesity may vary with age cross-sectionally and longitudinally among middle- and older-age African Americans (AAs) who experience a disproportionate burden of obesity-related health risks in the US [14].

As AAs are known to have relatively less of their body mass in their trunks and relatively more in their extremities compared to non-Hispanic whites [5], a better understanding of variations in age- and sex-related measures of adiposity among AA may suggest which anthropometric measure(s) may be better for monitoring obesity among elderly AA. In this study, we used data from the Jackson Heart Study (JHS), a community-based longitudinal study of cardiovascular diseases among adult AAs in Jackson, MS, to examine age- and sex-related variations in several anthropometric measures of obesity including BMI, WC, WHtR, and WHR, both cross-sectionally and longitudinally.

METHODS

Data Source

The JHS is the largest single-site, population-based cohort study of cardiovascular diseases in AAs. Participant recruitment for the JHS began in 2000, enrolling 5306 AAs from the tri-county area of the Jackson, MS metropolitan area. Participants were examined at baseline (V1 2000-2004) and two additional examinations (V2 2005-2008 and V3 2009-2013). Additional details of the JHS study design, recruitment and data collection have been published previously [15-17]. The JHS was approved by the IRB of the University of Mississippi Medical Center. Written informed consent was provided by all participants.

Analytic Sample

Because WHR data were only available at V2 and V3, for comparison purposes, anthropometric measures from V2 were used for the cross-sectional analysis of the variations in anthropometric measures by age. Anthropometric measures from V2 and V3 were used for the longitudinal analysis of changes in anthropometric measures due to aging effect. All participants who returned for V2 were included (N=4205). Participants who had missing values of any of the anthropometric measures of interest at V2 (N=142) or covariates (N=429) (physical activity-4; smoking status-60; education-5; alcohol consumption-21; nutritional intake-339) were excluded, leaving 3634 participants in the analytic sample. Of the 3634 participants included in the analytic sample, 3141 returned for V3 (86.4% retention rate).

Anthropometric Measures of Obesity

The anthropometric measures of obesity included BMI, WC, WHtR, and WHR. BMI was calculated as (weight (kg)/height (m)^2) [18]. WHtR was calculated as WC (cm)/height (cm) and WHR was calculated as WC (cm)/hip circumference (cm). Weight was measured to the nearest

0.1 kg and height to the nearest centimeter in light clothing and in stocking feet; WC was measured to the nearest centimeter at the umbilicus; hip circumference was measured to the nearest centimeter at the maximal protrusion. Obesity status (obese/non-obese) was classified based on cut-points recommended by guidelines or reported in the literature for each obesity measure as follows: BMI ≥ 30 (kg/m^2) [19]; WC > 88 cm for women or > 102 cm for men [20, 21]; WHtR ≥ 0.5 [22]; WHR ≥ 0.85 for women or ≥ 0.9 for men [23]. For comparison purposes, we computed sex-specific z-scores for each anthropometric measure to put them on the same scale, *i.e.*, in standardized (SD) unit, using the sex-specific means and standard deviations from the analytic sample (all V2 and V3 measurements were pooled to calculate the sex-specific means and standard deviations for each anthropometric measure).

Covariates

Covariates included education, physical activity, smoking status, alcohol consumption, and nutritional intake collected at V1 since they were not collected at V2. Education was based on self-reported years of schooling completed and included 3 categories: less than high school (<12 years), high school graduate or General Educational Development (GED), and attended vocational school, trade school, or college.

Smoking status, physical activity, and nutritional intake were self-reported. We used the American Heart Association (AHA) Life's Simple 7^{TM} classification to classify these lifestyle factors for analysis. AHA Life's Simple 7 is a metric developed by the American Heart Association defining ideal cardiovascular health: not smoking, regular physical activity, healthy diet, maintaining normal weight, and controlling cholesterol, blood pressure, and blood glucose levels. We used its definitions of "poor health," "intermediate health," and "ideal health" for controlling for lifestyle factors in the regression models. Smoking status was "poor" if the participant was a current smoker; "intermediate" if the participant had quit smoking less than a year prior to V1; "ideal" if the participant had never smoked or had quit smoking more than a year prior to V1. Physical activity was "poor" if the participant had zero minutes of moderate (3.00–5.99 kcals/kg/hour) or vigorous (≥ 6.00 kcals/kg/hour) leisure activity per week; "intermediate" if the participant did not have at least 150 minutes of moderate, or at least 75 minutes of vigorous, or at least 150 combined (moderate/vigorous) leisure activity per week; "ideal" if the participant had at least 150 minutes of moderate, or at least 75 minutes of vigorous, or at least 150 minutes of combined moderate/vigorous leisure activity per week. Nutritional intake was assessed for all participants using the short Delta Nutrition Intervention Research Initiative (Delta-NIRI) food frequency questionnaire (FFQ) with 158 items [24]. The five dietary components used to compute the AHA score, based on a 2000-kcal diet, were (1) fruits and vegetables, ≥ 4.5 cups/day; (2) non-fried fish, ≥ 2 3.5-ounce servings/week; (3) fiber-rich whole grains, ≥ 3 1-ounce servings/day; (4) sodium, ≤ 1,500 mg/day; and (5) sugar sweetened beverages, < 36 fluid ounces/week (≤ 450 kcal/week). "Ideal" diet was defined by a diet including 4–5 components; "intermediate" diet, 2–3 components; and "poor" diet, 0–1 component [25]. Alcohol consumption was dichotomized (yes/no) per participant's response to the question: "In the past 12 months, have you ever consumed an alcoholic beverage?"

Data Availability Statement

Requests for JHS data require approval of a JHS Manuscript Proposal or Ancillary Study Proposal. To protect the confidentiality and privacy of the JHS participants and their family, a Data and Materials Distribution Agreement (DMDA) is required to obtain data. To submit a request for data, complete a data request form at (https://redcap.umc.edu/surveys/?%20s=R48NR37HA8) [26].

Statistical Analysis

Cross-sectional analysis

Age at V2 was grouped into five age groups: <45, 45-<55, 55-<65, 65-<75, and 75+ years to examine the cross-sectional effect of age on anthropometric measures of obesity. The adjusted means of anthropometric measures (in SD unit) by age group were calculated and compared using linear regression models. All regression models were adjusted for sex, education, physical activity, smoking status, alcohol consumption, and nutritional intake. To examine whether the effect of age may be modified by sex, the significance of the sex*age group interaction term was tested by including the interaction term in the statistical models.

Longitudinal Analysis

The longitudinal effect of age (*i.e.*, the effect of aging) on anthropometric measures of obesity was examined by analyzing the change in anthropometric measures (in SD unit) from V2 to V3 (V3 minus V2 measures) versus follow-up time between V2 and V3 (average 3.3 years, range 1.8 to 6.5 years). Follow-up time was rescaled as 5-year increment so that the regression coefficient reflects a change across 5 years. All analyses were stratified by age group at V2 and sex, and performed using mixed effects models with random intercept (individuals) and random slope (follow-up time). All regression models were adjusted for age, education, physical activity, smoking status, alcohol consumption, and nutritional intake. The significance of the modifying effect of sex was tested by including a sex*follow-up time interaction term in the statistical models.

All reported *P* values correspond to 2-tailed tests and were significant at the 0.05 level. Analyses were performed using Stata/SE 17.0.

Participant Involvement

Participants who met eligibility requirements were asked to bring their family members for the family study, but they were not directly involved in recruitment, or any other steps in this research process. Participants are sent lay summaries of the results of published manuscripts that derived from the JHS. Lay summaries of study findings are also disseminated to the general community and participants at JHS events [26].

RESULTS

Participant characteristics

Table 1 shows the characteristics of participants in the analytic sample. The mean age of the participants was 59.4 ± 12.0 years old (range 25-97) and about 65% were women. Over 85% of the participants had at least a high school education or GED. Compared to younger participants, older participants were more likely to be women, had less than high school education, and reported lower levels of physical activity. Older participants were also more likely to have ideal smoking status and nutritional intake and never consumed alcohol beverages in the last 12 months.

The mean (SD) of anthropometric measures were as follows: weight 90.9 (21.0) kg, height 168.5 (9.4) cm, WC 102.0 (15.7) cm, hip circumference 114.2 (14.4) cm, BMI 32.0 (7.1) kg/m2, WHtR 0.61 (0.10), and WHR 0.89 (0.08).The prevalence of obesity defined by BMI, WC, WHtR, and WHR were 55%, 68%, 91%, and 64% respectively. Compared to younger participants, anthropometric measures were generally lower in older participants, except for WHtR and WHR, which were higher in older participants. For WC, the largest WC was observed in the 55-< 65 and the 65-< 75 years groups and the smallest in the 75+ years group.

For obesity, the prevalence of obesity increased with age when defined by WHtR (from 86% in 25-< 45 years group to 94% in 75+ years group) and WHR (from 48% in 25- < 45 years old group to 78% in 75+ years group). While the prevalence of obesity defined by BMI generally decreased with age from 63% in 25-< 45 years group to 41% in 75+ years group.

Cross-sectional analysis

Table 2 shows the results of the cross-sectional analysis of standardized anthropometric measures of obesity by age group from linear regression models adjusting for covariates. For BMI and WC, there was an inverse relationship with age, whereas WHR showed a positive relationship with age. For example, the adjusted mean BMI was 0.80 SD unit lower in the oldest age group than in the youngest age group (β (95% CI) -0.80 (-0.94, -0.66)). In contrast, the

Table 1. Characteristics of Jackson Heart Study Participants included in the Analytic Sample

		Age (years)				
Characteristics	**Total**	**25-< 45**	**45-< 55**	**55-< 65**	**65-< 75**	**75+**
Sample Size	3634	415	884	994	941	400
Age (years), mean (SD)	59.4 (12.0)	39.4 (4.8)	49.7 (2.9)	59.5 (3.0)	69.0 (2.8)	78.9 (3.5)
Sex, n (%)						
Women	2362 (65%)	257 (62%)	557 (63%)	644 (65%)	627 (67%)	277 (69%)
Men	1272 (35%)	158 (38%)	327 (37%)	350 (35%)	314 (33%)	123 (31%)
Education, n (%)*						
Less than high school	552 (15%)	8 (2%)	39 (4%)	94 (9%)	245 (26%)	166 (42%)
High school graduate/GED	685 (19%)	69 (17%)	135 (15%)	173 (17%)	224 (24%)	84 (21%)
Attended vocational school, trade school, or college	2397 (66%)	338 (81%)	710 (80%)	727 (73%)	472 (50%)	150 (38%)
Physical Activity, n (%)*						
Poor	1718 (47%)	137 (33%)	360 (41%)	460 (46%)	513 (55%)	248 (62%)
Intermediate	1198 (33%)	166 (40%)	324 (37%)	331 (33%)	276 (29%)	101 (25%)
Ideal	718 (20%)	112 (27%)	200 (23%)	203 (20%)	152 (16%)	51 (13%)
Smoking Status, n (%)*						
Poor	397 (11%)	38 (9%)	111 (13%)	132 (13%)	100 (11%)	16 (4%)
Intermediate	37 (1%)	3 (1%)	16 (2%)	11 (1%)	6 (1%)	1 (0%)
Ideal	3200 (88%)	374 (90%)	757 (86%)	851 (86%)	835 (89%)	383 (96%)
Nutritional intake, n (%)*						
Poor	2460 (68%)	339 (82%)	676 (76%)	634 (64%)	575 (61%)	236 (59%)
Intermediate	1117 (31%)	75 (18%)	205 (23%)	338 (34%)	345 (37%)	154 (39%)
Ideal	57 (2%)	1 (0%)	3 (0%)	22 (2%)	21 (2%)	10 (3%)
Alcohol Consumption, n (%)*						

		Age (years)				
Characteristics	**Total**	**25-< 45**	**45-< 55**	**55-< 65**	**65-< 75**	**75+**
Yes	1672 (46%)	247 (60%)	524 (59%)	490 (49%)	328 (35%)	83 (21%)
No	1962 (54%)	168 (40%)	360 (41%)	504 (51%)	613 (65%)	317 (79%)
Anthropometric measures, mean (SD)						
Weight (kg)	90.9 (21.0)	98.2 (26.2)	93.3 (22.0)	92.2 (19.8)	88.2 (18.3)	81.1 (17.0)
Height (cm)	168.5 (9.4)	169.8 (9.5)	169.7 (9.2)	169.1 (9.5)	167.6 (8.9)	165.4 (9.7)
WC (cm)	102.0 (15.7)	102.6(18.9)	100.9 (16.0)	103.0 (15.3)	102.6 (15.)	100.5 (13.6)
Hip Circumference (cm)	114.2 (14.4)	117.3 (16.5)	114.8 (14.8)	114.8 (14.1)	113.2 (13.)	110.4 (12.8)
BMI (kg/m^2)	32.0 (7.1)	34.1 (9.1)	32.4 (7.3)	32.3 (6.8)	31.4 (6.3)	29.6 (5.7)
WHtR	0.61 (0.10)	0.61 (0.11)	0.60 (0.10)	0.61 (0.09)	0.61 (0.09)	0.61 (0.08)
WHR	0.89 (0.08)	0.87 (0.08)	0.88 (0.08)	0.90 (0.08)	0.91 (0.08)	0.91 (0.07)
Obesity, n (%)						
Defined by BMI						
Yes	2013 (55%)	260 (63%)	502 (57%)	588 (59%)	498 (53%)	165 (41%)
No	1621 (45%)	155 (37%)	382 (43%)	406 (41%)	443 (47%)	235 (59%)
Defined by WC						
Yes	2484 (68%)	266 (64%)	572 (65%)	710 (71%)	661 (70%)	275 (69%)
No	1150 (32%)	149 (36%)	312 (35%)	284 (29%)	280 (30%)	125 (31%)
Defined by WHtR						
Yes	3297 (91%)	356 (86%)	775 (88%)	910 (92%)	882 (94%)	374 (94%)
No	337 (9%)	59 (14%)	109 (12%)	84 (8%)	59 (6%)	26 (7%)
Defined by WHR						
Yes	2336 (64%)	201 (48%)	480 (54%)	664 (67%)	678 (72%)	313 (78%)
No	1298 (36%)	214 (52%)	404 (46%)	330 (33%)	263 (28%)	87 (22%)

*denotes data collected at V1 were used. All other characteristics were based on data collected at V2.

SD=standard deviation; GED=General Educational Development; BMI=body mass index; WC=waist circumference; WHtR=waist-to-height ratio; WHR=waist-to-hip ratio.

Table 2. Cross-sectional Analysis of Standardized Anthropometric Measures at V2 by Age Group

	Age (years)					
Anthropometric Measures	**25-<45 (Ref)** β (95% CI)*	**45-<55** β (95% CI)	**55-<65** β (95% CI)	**65-<75** β (95% CI)	**75+** β (95% CI)	**p-value for trend**
BMI	0	-0.25 (-0.37, -0.14)	-0.31 (-0.42, -0.20)	-0.48 (-0.60, -0.36)	-0.80 (-0.94, -0.66)	<.0001
WC	0	-0.12 (-0.24, -0.00)	-0.01 (-0.12, 0.11)	-0.09 (-0.21, 0.03)	-0.27 (-0.41, -0.13)	0.018
WHtR	0	-0.12 (-0.24, -0.01)	-0.0 1(-0.12, 0.11)	-0.05 (-0.17, 0.07)	-0.18 (-0.32, -0.03)	0.325
WHR	0	0.08 (-0.03, 0.20)	0.35 (0.23, 0.46)	0.43 (0.31, 0.55)	0.48 (0.33, 0.62)	<.0001

*β coefficient and 95% confidence interval (CI) from linear regression models, adjusting for sex, education, physical activity, smoking status, alcohol consumption, and nutritional intake.

BMI=body mass index; WC=waist circumference; WHtR=waist-to-height ratio; WHR=waist-to-hip ratio. CI: Confidence Interval; Ref: reference group.

adjusted mean WHR was close to half SD unit higher in the oldest age group than in the youngest age group (β (95% CI) 0.48(0.33,0.62)). The tests for trend for BMI, WC and WHR were statistically significant ($p<.05$). No statistically significant sex*age interactions were observed (Supplemental Table 1).

Longitudinal analysis

Figure 1 depicts the anthropometric data for longitudinal analysis by sex and age group (< 45, 45-< 55, 55-< 65, 65-< 75, and 75+ years at V2). The mean anthropometric measures of obesity at V2 and V3 were calculated and plotted against the mean age at the respective visits. As shown in Figure 1, the mean BMI and WHtR were higher in women than in men, while the mean WC and WHR were lower in women than in men across time and in all age groups.

Figure 2 shows the results of changes in standardized anthropometric measures of obesity per every 5 years increase in age (aging) from mixed effects models adjusting for covariates, by sex and age group. A positive coefficient (*i.e.*, on the right side of the vertical reference line at '0') indicates an increasing trend with aging and a negative coefficient indicates a decreasing trend with aging. As shown in Figure 2, aging was associated with increased BMI, WC, and WHtR among younger age groups, but the increasing trend tended to be diminished or reversed among older age groups in both sexes. For example, for BMI, 5 year aging was associated with increase of 0.13 (0.06, 0.20) SD units in BMI in age groups 25-< 45 and 0.09 (0.05, 0.14) SD units in 45-< 55 years , but the trend reversed in age groups 65 years or older with decrease of -0.07 (-0.10, -0.03) SD units in age group of 65-< 75 years, and -0.14 (-0.19, -0.09) SD units in 75+ years among women (Figure 2a). On the other hand, WHR tended to increase with aging across all sex and age groups, although the magnitude of the increasing trend generally decreased in older age groups. For instance, with each 5-year of aging, the mean WHR increased by 0.74 (0.52, 0.97) SD units for 25-< 45 years, 0.51 (0.39, 0.62) SD units for 45-< 55 years, 0.50 (0.38, 0.62) SD units for 55-< 65 years, 0.47 (0.34, 0.59) SD units for 65-< 75 years, and 0.24 (0.05, 0.44) SD units for 75+ years among male. Additionally, WHR had the highest SD unit increase with aging among the four anthropometric measures of obesity examined. For instance, among men 45 years and younger, the mean WHR increased by 0.74 (95% CI 0.52, 0.97) SD unit with each 5-year of aging, while the mean BMI, WC, and WHtR increased only by 0.14 (0.05, 0.23), 0.28 (0.16, 0.40), and 0.30 (0.17, 0.42) SD unit, respectively. Statistically significant sex*age interactions were observed in the analysis for WHR among 25-< 45 years group and WC among 45-< 55 years group (Supplemental Table 2) although they were in the same direction, but different magnitudes of the increasing trend among different sexes (Figure 2).

DISCUSSION

In this study of a large sample of adult AA men and women in Jackson, MS, we found that in cross-sectional analyses, compared to the younger age group, the older age group had a lower mean BMI, WC, and WHtR, but a higher mean WHR. In longitudinal analyses, the effect of aging on the changes in BMI, WC, and WHtR was similar; with the mean values increasing with age only among younger groups. In contrast, the mean WHR increased with age across all age groups.

The observation that BMI, WC and WHtR decreased with age while WHR increased with age in the older age group suggests that loss of lean muscle mass or change in the distribution of fat and lean mass with age may play an important role in disease risks associated with obesity in older adults. This may also partially explain why older adults considered to be overweight based on BMI have a lower mortality rate than those with lower BMI (the "obesity paradox") [27]. In a prospective cohort study among male health professionals in the US, a significant positive monotonic association between predicted fat mass and all-cause mortality, and a U-shaped association between predicted lean body mass and all-cause mortality were found, suggesting that the "obesity paradox" may be largely caused by low lean body mass, instead of low-fat mass, in the lower BMI range [28]. In another prospective cohort study of older British men, it was found that sarcopenia and central adiposity were associated with higher all-cause mortality [29]. In our own analyses in the JHS, we found the relationships between BMI, WC, WHtR and overall mortality to be J-shaped whereas there was a monotonic increasing relationship between WHR and overall mortality, suggesting once corrected for gluteal muscle mass, lower BMI or central adiposity does not afford greater mortality risks [30]. Aging is related to muscle loss and visceral fat accumulation, and has been associated with several cardio-metabolic chronic diseases and mortality [31]. Therefore, anthropometric measures and aging are together key risk factors of chronic diseases and mortality. This analyses further reveal the relationship between the two risk factors, and explains the rationale behind the relationships among risk factors and mortality in AA adults. These findings with WHR fit well with the postulated biological changes in old age, including redistribution of adiposity from limbs to visceral with concomitant loss of lean muscle mass, as approximated by waist circumference (central adiposity) and hip circumferences (gluteal muscle), respectively [23]. Therefore, WHR has been reported to be a better predictor of obesity-related risk among older adults than BMI and WC [32, 33]. The strengths of this study include the large sample size and longitudinal follow-up of a well-characterized cohort of adult AAs, including a substantial proportion of elderly men and women with anthropometric measures of obesity across two visits, and a relatively high retention rate (86%) across visits. However, this study has several limitations. First, the longitudinal change in anthropometric measures over the life-course were derived from participants from different birth cohorts. While it is reasonable to assume that the longitudinal trend observed in anthropometric measures may be consistent with the biology of aging irrespective of birth cohort, we cannot be certain without longer term follow-up of participants of the same birth cohort. Furthermore, the anthropometric measures from V2 and V3 were used for the analysis, while the covariates including education, physical activity, smoking status, alcohol consumption, and nutritional intake collected at V1 were used for the analysis since they were not collected at V2. In addition, the results may not be generalizable to all AA adults across the US, as the sample was drawn solely from residents of Jackson, MS.

CONCLUSION

Our results showed that among middle age AA adults, all four anthropometric measures of obesity examined (BMI, WC, WHtR, and WHR) increased with aging. However, among elderly AA adults, WHR was the only anthropometric measures that showed continued increase with aging. Our findings suggest that WHR, a measure that captures both central adiposity and body composition, may be an important anthropometric measure to collect to monitor obesity and obesity-related health risks among older AA adults. These findings should be verified in other ethnically diverse populations.

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DISCLAIMER

The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the National Heart, Lung, and Blood Institute; the National Institute for

Minority Health and Health Disparities; the National Institutes of Health; or the U.S. Department of Health and Human Services.

AUTHORS' CONTRIBUTIONS

YG–analysis and interpretation of data, drafting and final approval of the manuscript; YM–statistical expertise, helped conduct the literature review, critical review and final approval of the manuscript; RAB– critical review and final approval of the manuscript; AGB– critical review and final approval of the manuscript; AC–conception and design of study, critical review and final approval of manuscript. All authors have read and approved the manuscript.

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AVAILABILITY OF DATA AND MATERIALS

As a National Heart, Lung, and Blood Institute (NHLBI)-funded study, the JHS follows the NHLBI's policy for data sharing, which includes depositing the data into the NHLBI's Biologic Specimen and Data Repository Information Coordinating Center (BioLINCC) to make it publicly available to other investigators. The link to the JHS dataset: https://biolincc.nhlbi.nih.gov/studies/jhs/. Download directions are provided on the website. NHLBI further requires the JHS to maintain the accuracy of this dataset, so the JHS Coordinating Center sends modifications to BioLINCC for incorporation as appropriate. Privacy and access settings are controlled by BioLINCC, and the investigators have no influence on these settings.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study was approved by the Institutional Review Board of the University of Mississippi Medical Center (UMMC IRB Tracking Number: 1998-6004; DHHS FWA: 00003630 0000043; IORG: 00000061; IRB Registration: 00005033) and participants provided written informed consent. The JHS is an observational cohort study. No experiments were performed in the study.

PATIENT CONSENT FOR PUBLICATION

Not applicable.

COMPETING INTERESTS

None.

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Legend/caption for Figures

Figure 1's title: Figure 1(a)-(d). Mean anthropometric measures values at V2 to V3 by age-group and sex.

Figure 1's brief explanation: Each line shows the changes of unadjusted mean anthropometric measure from V2 to V3 for each age group stratified by sex.

yrs=years.

Figure 2's title: Figure 2(a)-(d). Longitudinal analyses of changes of standardized anthropometric measures per 5-year aging by sex and age group.

Figure 2's brief explanation: Mixed effects models with random intercept and random slope were used to test aging effect. Models were adjusted for covariates collected at V1, including age, education, physical activity, smoking status, alcohol consumption, and nutritional intake.

M=male; F=female; yrs=years; CI=Confidence Interval.

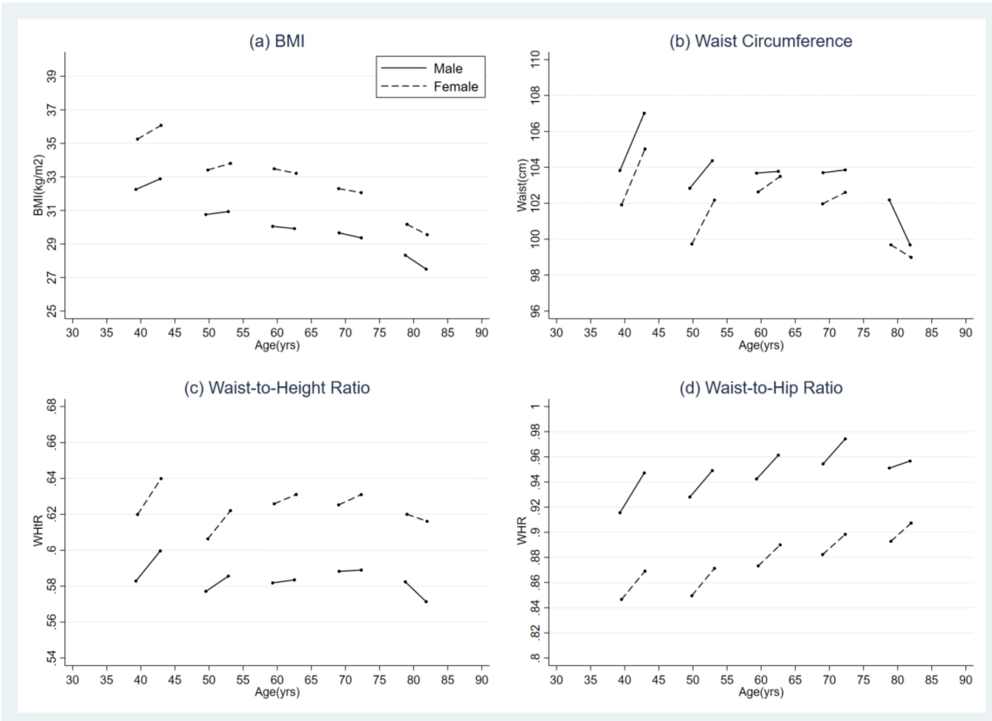

Figure 1(a)-(d). Mean anthropometric measures values at V2 to V3 by age-group and sex.
Each line shows the changes of unadjusted mean anthropometric measure from V2 to V3 for each age group stratified by sex.
yrs=years.

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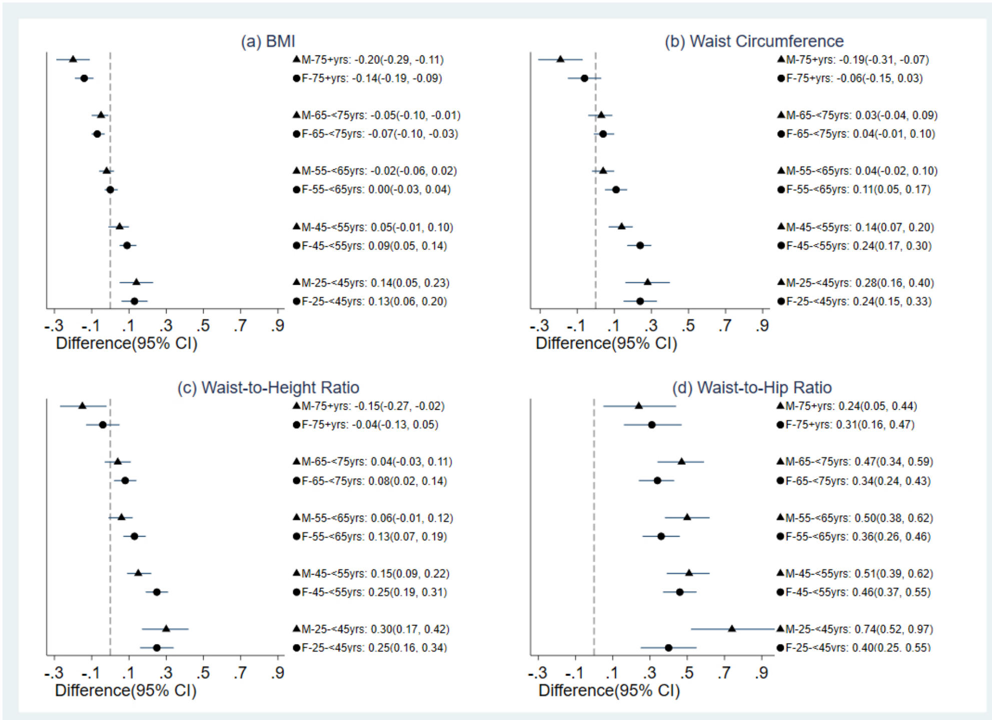

Figure 2(a)-(d). Longitudinal analyses of changes of standardized anthropometric measures per 5-year aging by sex and age group.
Mixed effects models with random intercept and random slope were used to test aging effect. Models were adjusted for covariates collected at V1, including age, education, physical activity, smoking status, alcohol consumption, and nutritional intake.
M=male; F=female; yrs=years; CI=Confidence Interval.

190x138mm (144 x 144 DPI)

Supplemental Table 1. P-values for effect modification by sex on the associations between obesity measures and age group in cross-sectionally analysis.

Anthropometric Measures	**P-value for effect modification by sex**
BMI	0.917
WC	0.869
WHtR	0.815
WHR	0.691

The sex*age group interaction term was included in linear regression models adjusting for sex, education, physical activity, smoking status, alcohol consumption, and nutritional intake.
BMI=body mass index; WC=waist circumference; WHtR=waist-to-height ratio; WHR=waist-to-hip ratio.

Supplemental Table 2. P-values for effect modification by sex on the associations between obesity measures and aging in each age group in longitudinal analysis.

Anthropometric Measures	**25-<45 yrs.**	**45-<55 yrs.**	**55-<65 yrs.**	**65-<75 yrs.**	**75+ yrs.**
BMI	0.929	0.160	0.475	0.726	0.281
WC	0.657	0.050	0.157	0.792	0.100
WHtR	0.604	0.051	0.139	0.418	0.187
WHR	0.007	0.534	0.082	0.119	0.602

The sex*follow-up time interaction term was included in mixed effects models with random intercept and random slope were used to test aging effect. Models were adjusted for covariates including education, physical activity, smoking status, alcohol consumption, and nutritional intake.
BMI=body mass index; WC=waist circumference; WHtR=waist-to-height ratio; WHR=waist-to-hip ratio; yrs.= years.

STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*

Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1-2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2-3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	3	State specific objectives, including any pre-specified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	6
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	n/a
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6-8
Bias	9	Describe any efforts to address potential sources of bias	n/a
Study size	10	Explain how the study size was arrived at	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7-8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	9
		(*b*) Describe any methods used to examine subgroups and interactions	9
		(*c*) Explain how missing data were addressed	n/a
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed	n/a

		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	n/a
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6
		(b) Give reasons for non-participation at each stage	n/a
		(c) Consider use of a flow diagram	n/a
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	10
		(b) Indicate number of participants with missing data for each variable of interest	n/a
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	n/a
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	n/a
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	n/a
		Cross-sectional study—Report numbers of outcome events or summary measures	11-15
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	11-16
		(*b*) Report category boundaries when continuous variables were categorized	n/a
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	n/a
Discussion			
Key results	18	Summarise key results with reference to study objectives	16-17
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	18
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	16-18
Generalisability	21	Discuss the generalisability (external validity) of the study results	18
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	19

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Cross-sectional and Longitudinal Analyses of Variations of Anthropometric Measures of Obesity with Age in The Jackson Heart Study

Running Title: Obesity and Age

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ABSTRACT

Objective To explore how anthropometric measures of obesity vary with age among African American (AA) adults.

Participants and setting 3634 AA adults participated in the Jackson Heart Study (Jackson, MS) from 2004 to 2013. .

Outcome measures Body mass index (BMI), waist circumference (WC), waist-to-height ratio (WHtR), and waist-to-hip ratio (WHR).

Methods Linear regression models were used to estimate the mean differences in anthropometric measures cross-sectionally by age group. Longitudinal changes in anthropometric measures over time (*i.e.*, the aging effect) within each sex and age group were analyzed using mixed effects models. All regression models were adjusted for education and lifestyle factors.

Results In cross-sectional analysis, older age was associated with lower BMI, WC, and WHtR, but higher WHR in both sexes. Compared with 25-<44 years age group, the mean (95% CI) BMI, WC, and WHtR was 0.80 (0.66, 0.94), 0.27 (0.13, 0.42), and 0.18 (0.03, 0.32) standardized (SD) unit lower, while WHR was 0.48 (0.33, 0.62) SD unit higher in the 75+ years age group. In longitudinal analysis, aging was associated with increased BMI, WC, and WHtR, among younger age groups but not in older age groups. However, WHR tended to increase with aging across all age groups in both sexes. Among men 75+ years old, the mean change (95% CI) in BMI, WC, and WHtR for every 5 years increase in age, was -0.20 (-0.29, -0.11), -0.19 (-0.31, -0.07), -0.15 (-0.27, -0.02) SD unit, respectively, while it was 0.24 (0.05, 0.44) SD unit for WHR.

Conclusions Among middle-aged AA adults, all four anthropometric measures of obesity examined increased with aging. However, among elderly AA adults, only WHR showed

continued increase with aging. WHR may be a better anthropometric measure for monitoring obesity in older AA adults.

Key words: age, aging, anthropometric measures, obesity, body mass index, waist circumference, waist-to-height ratio, waist-to-hip ratio

STRENGTHS AND LIMITATIONS OF THIS STUDY

- The strengths of this study include the large sample size and longitudinal follow-up of a well-characterized cohort of AA adults.
- The longitudinal change in anthropometric measures over the life-course were derived from participants from different birth cohorts.
- The anthropometric measures from V2 and V3 were used for the analysis, while the covariates used for the analysis were collected at V1.
- The results of this study may not be generalizable to all AA adults across the US.

INTRODUCTION

Ongoing monitoring of trends in obesity is a global health priority due to increased prevalence of obesity worldwide and its associated morbidity and mortality, trans-generational effects, and disproportionate burden in disadvantaged populations [1-4]. Reports of variations in prevalence of obesity by age, sex, and race/ethnicity are helpful for obesity-related risk stratification as the body distribution of adiposity appears to vary by demographic characteristics [5]. However, to date, the literature on trends in obesity by demographic characteristics has focused on age- and sex-variations in prevalence of obesity defined by one anthropometric measure only (e.g., BMI, WC, or WHtR) [6 -11], or on comparisons of several anthropometric measures of obesity among select population subgroups [12, 13]. From public health and clinical monitoring perspectives, an important knowledge gap emerging from this work on trends in obesity across population subgroups is how anthropometric measures of obesity may vary with age cross-sectionally and longitudinally among middle- and older-age African Americans (AAs) who experience a disproportionate burden of obesity-related health risks in the US [14].

As AAs are known to have relatively less of their body mass in their trunks and relatively more in their extremities compared to non-Hispanic whites [5], a better understanding of variations in age- and sex-related measures of adiposity among AA may suggest which anthropometric measure(s) may be better for monitoring obesity among elderly AA. In this study, we used data from the Jackson Heart Study (JHS), a community-based longitudinal study of cardiovascular diseases among adult AAs in Jackson, MS, to examine age- and sex-related variations in several anthropometric measures of obesity including BMI, WC, WHtR, and WHR, both cross-sectionally and longitudinally.

METHODS

Data Source

The JHS is the largest single-site, population-based cohort study of cardiovascular diseases in AAs. Participant recruitment for the JHS began in 2000, enrolling 5306 AAs from the tri-county area of the Jackson, MS metropolitan area. Participants were examined at baseline (V1 2000-2004) and two additional examinations (V2 2005-2008 and V3 2009-2013). Additional details of the JHS study design, recruitment and data collection have been published previously [15-17]. The JHS was approved by the IRB of the University of Mississippi Medical Center. Written informed consent was provided by all participants.

Analytic Sample

Because WHR data were only available at V2 and V3, for comparison purposes, anthropometric measures from V2 were used for the cross-sectional analysis of the variations in anthropometric measures by age. Anthropometric measures from V2 and V3 were used for the longitudinal analysis of changes in anthropometric measures due to aging effect. All participants who returned for V2 were included (N=4205). Participants who had missing values of any of the anthropometric measures of interest at V2 (N=142) or covariates (N=429) (physical activity-4; smoking status-60; education-5; alcohol consumption-21; nutritional intake-339) were excluded, leaving 3634 participants in the analytic sample. Of the 3634 participants included in the analytic sample, 3141 returned for V3 (86.4% retention rate).

Anthropometric Measures of Obesity

The anthropometric measures of obesity included BMI, WC, WHtR, and WHR. BMI was calculated as (weight (kg)/height (m)^2) [18]. WHtR was calculated as WC (cm)/height (cm) and WHR was calculated as WC (cm)/hip circumference (cm). Weight was measured to the nearest

0.1 kg and height to the nearest centimeter in light clothing and in stocking feet; WC was measured to the nearest centimeter at the umbilicus; hip circumference was measured to the nearest centimeter at the maximal protrusion. Obesity status (obese/non-obese) was classified based on cut-points recommended by guidelines or reported in the literature for each obesity measure as follows: BMI ≥ 30 (kg/m^2) [19]; WC > 88 cm for women or > 102 cm for men [20, 21]; WHtR ≥ 0.5 [22]; WHR ≥ 0.85 for women or ≥ 0.9 for men [23]. For comparison purposes, we computed sex-specific z-scores for each anthropometric measure to put them on the same scale, *i.e.*, in standardized (SD) unit, using the sex-specific means and standard deviations from the analytic sample (all V2 and V3 measurements were pooled to calculate the sex-specific means and standard deviations for each anthropometric measure).

Covariates

Covariates included education, physical activity, smoking status, alcohol consumption, and nutritional intake collected at V1 since they were not collected at V2. Education was based on self-reported years of schooling completed and included 3 categories: less than high school (<12 years), high school graduate or General Educational Development (GED), and attended vocational school, trade school, or college.

Smoking status, physical activity, and nutritional intake were self-reported. We used the American Heart Association (AHA) Life's Simple 7™ classification to classify these lifestyle factors for analysis. AHA Life's Simple 7 is a metric developed by the American Heart Association defining ideal cardiovascular health: not smoking, regular physical activity, healthy diet, maintaining normal weight, and controlling cholesterol, blood pressure, and blood glucose levels. We used its definitions of "poor health," "intermediate health," and "ideal health" for controlling for lifestyle factors in the regression models. Smoking status was "poor" if the participant was a current smoker; "intermediate" if the participant had quit smoking less than a year prior to V1; "ideal" if the participant had never smoked or had quit smoking more than a year prior to V1. Physical activity was "poor" if the participant had zero minutes of moderate (3.00–5.99 kcals/kg/hour) or vigorous (≥ 6.00 kcals/kg/hour) leisure activity per week; "intermediate" if the participant did not have at least 150 minutes of moderate, or at least 75 minutes of vigorous, or at least 150 combined (moderate/vigorous) leisure activity per week; "ideal" if the participant had at least 150 minutes of moderate, or at least 75 minutes of vigorous, or at least 150 minutes of combined moderate/vigorous leisure activity per week. Nutritional intake was assessed for all participants using the short Delta Nutrition Intervention Research Initiative (Delta-NIRI) food frequency questionnaire (FFQ) with 158 items [24]. The five dietary components used to compute the AHA score, based on a 2000-kcal diet, were (1) fruits and vegetables, ≥ 4.5 cups/day; (2) non-fried fish, ≥ 2 3.5-ounce servings/week; (3) fiber-rich whole grains, ≥ 3 1-ounce servings/day; (4) sodium, ≤ 1,500 mg/day; and (5) sugar sweetened beverages, < 36 fluid ounces/week (≤ 450 kcal/week). "Ideal" diet was defined by a diet including 4–5 components; "intermediate" diet, 2–3 components; and "poor" diet, 0–1 component [25]. Alcohol consumption was dichotomized (yes/no) per participant's response to the question: "In the past 12 months, have you ever consumed an alcoholic beverage?"

Data Availability Statement

Requests for JHS data require approval of a JHS Manuscript Proposal or Ancillary Study Proposal. To protect the confidentiality and privacy of the JHS participants and their family, a Data and Materials Distribution Agreement (DMDA) is required to obtain data. To submit a request for data, complete a data request form at (https://redcap.umc.edu/surveys/?%20s=R48NR37HA8) [26].

Statistical Analysis

Cross-sectional analysis

Age at V2 was grouped into five age groups: <45, 45-<55, 55-<65, 65-<75, and 75+ years to examine the cross-sectional effect of age on anthropometric measures of obesity. The adjusted means of anthropometric measures (in SD unit) by age group were calculated and compared using linear regression models. All regression models were adjusted for sex, education, physical activity, smoking status, alcohol consumption, and nutritional intake. To examine whether the effect of age may be modified by sex, the significance of the sex*age group interaction term was tested by including the interaction term in the statistical models.

Longitudinal Analysis

The longitudinal effect of age (*i.e.*, the effect of aging) on anthropometric measures of obesity was examined by analyzing the change in anthropometric measures (in SD unit) from V2 to V3 (V3 minus V2 measures) versus follow-up time between V2 and V3 (average 3.3 years, range 1.8 to 6.5 years). Follow-up time was rescaled as 5-year increment so that the regression coefficient reflects a change across 5 years. All analyses were stratified by age group at V2 and sex, and performed using mixed effects models with random intercept (individuals) and random slope (follow-up time). All regression models were adjusted for age, education, physical activity, smoking status, alcohol consumption, and nutritional intake. The significance of the modifying effect of sex was tested by including a sex*follow-up time interaction term in the statistical models.

All reported P values correspond to 2-tailed tests and were significant at the 0.05 level. Analyses were performed using Stata/SE 17.0.

Participant Involvement

Participants who met eligibility requirements were asked to bring their family members for the family study, but they were not directly involved in recruitment, or any other steps in this research process. Participants are sent lay summaries of the results of published manuscripts that derived from the JHS. Lay summaries of study findings are also disseminated to the general community and participants at JHS events [26].

RESULTS

Participant characteristics

Table 1 shows the characteristics of participants in the analytic sample. The mean age of the participants was 59.4 ± 12.0 years old (range 25-97) and about 65% were women. Over 85% of the participants had at least a high school education or GED. Compared to younger participants, older participants were more likely to be women, had less than high school education, and reported lower levels of physical activity. Older participants were also more likely to have ideal smoking status and nutritional intake and never consumed alcohol beverages in the last 12 months.

The mean (SD) of anthropometric measures were as follows: weight 90.9 (21.0) kg, height 168.5 (9.4) cm, WC 102.0 (15.7) cm, hip circumference 114.2 (14.4) cm, BMI 32.0 (7.1) kg/m2, WHtR 0.61 (0.10), and WHR 0.89 (0.08).The prevalence of obesity defined by BMI, WC, WHtR, and WHR were 55%, 68%, 91%, and 64% respectively. Compared to younger participants, anthropometric measures were generally lower in older participants, except for WHtR and WHR, which were higher in older participants. For WC, the largest WC was observed in the 55-< 65 and the 65-< 75 years groups and the smallest in the 75+ years group.

For obesity, the prevalence of obesity increased with age when defined by WHtR (from 86% in 25-< 45 years group to 94% in 75+ years group) and WHR (from 48% in 25- < 45 years old group to 78% in 75+ years group). While the prevalence of obesity defined by BMI generally decreased with age from 63% in 25-< 45 years group to 41% in 75+ years group.

Cross-sectional analysis

Table 2 shows the results of the cross-sectional analysis of standardized anthropometric measures of obesity by age group from linear regression models adjusting for covariates. For BMI and WC, there was an inverse relationship with age, whereas WHR showed a positive relationship with age. For example, the adjusted mean BMI was 0.80 SD unit lower in the oldest age group than in the youngest age group (β (95% CI) -0.80 (-0.94, -0.66)). In contrast, the

Table 1. Characteristics of Jackson Heart Study Participants included in the Analytic Sample

		Age (years)				
Characteristics	**Total**	**25-< 45**	**45-< 55**	**55-< 65**	**65-< 75**	**75+**
Sample Size	3634	415	884	994	941	400
Age (years), mean (SD)	59.4 (12.0)	39.4 (4.8)	49.7 (2.9)	59.5 (3.0)	69.0 (2.8)	78.9 (3.5)
Sex, n (%)						
Women	2362 (65%)	257 (62%)	557 (63%)	644 (65%)	627 (67%)	277 (69%)
Men	1272 (35%)	158 (38%)	327 (37%)	350 (35%)	314 (33%)	123 (31%)
Education, n (%)*						
Less than high school	552 (15%)	8 (2%)	39 (4%)	94 (9%)	245 (26%)	166 (42%)
High school graduate/GED	685 (19%)	69 (17%)	135 (15%)	173 (17%)	224 (24%)	84 (21%)
Attended vocational school, trade school, or college	2397 (66%)	338 (81%)	710 (80%)	727 (73%)	472 (50%)	150 (38%)
Physical Activity, n (%)*						
Poor	1718 (47%)	137 (33%)	360 (41%)	460 (46%)	513 (55%)	248 (62%)
Intermediate	1198 (33%)	166 (40%)	324 (37%)	331 (33%)	276 (29%)	101 (25%)
Ideal	718 (20%)	112 (27%)	200 (23%)	203 (20%)	152 (16%)	51 (13%)
Smoking Status, n (%)*						
Poor	397 (11%)	38 (9%)	111 (13%)	132 (13%)	100 (11%)	16 (4%)
Intermediate	37 (1%)	3 (1%)	16 (2%)	11 (1%)	6 (1%)	1 (0%)
Ideal	3200 (88%)	374 (90%)	757 (86%)	851 (86%)	835 (89%)	383 (96%)
Nutritional intake, n (%)*						
Poor	2460 (68%)	339 (82%)	676 (76%)	634 (64%)	575 (61%)	236 (59%)
Intermediate	1117 (31%)	75 (18%)	205 (23%)	338 (34%)	345 (37%)	154 (39%)
Ideal	57 (2%)	1 (0%)	3 (0%)	22 (2%)	21 (2%)	10 (3%)
Alcohol Consumption, n (%)*						

		Age (years)				
Characteristics	**Total**	**25-< 45**	**45-< 55**	**55-< 65**	**65-< 75**	**75+**
Yes	1672 (46%)	247 (60%)	524 (59%)	490 (49%)	328 (35%)	83 (21%)
No	1962 (54%)	168 (40%)	360 (41%)	504 (51%)	613 (65%)	317 (79%)
Anthropometric measures, mean (SD)						
Weight (kg)	90.9 (21.0)	98.2 (26.2)	93.3 (22.0)	92.2 (19.8)	88.2 (18.3)	81.1 (17.0)
Height (cm)	168.5 (9.4)	169.8 (9.5)	169.7 (9.2)	169.1 (9.5)	167.6 (8.9)	165.4 (9.7)
WC (cm)	102.0 (15.7)	102.6(18.9)	100.9 (16.0)	103.0 (15.3)	102.6 (15.[illegible])	100.5 (13.6)
Hip Circumference (cm)	114.2 (14.4)	117.3 (16.5)	114.8 (14.8)	114.8 (14.1)	113.2 (13.[illegible])	110.4 (12.8)
BMI (kg/m^2)	32.0 (7.1)	34.1 (9.1)	32.4 (7.3)	32.3 (6.8)	31.4 (6.3)	29.6 (5.7)
WHtR	0.61 (0.10)	0.61 (0.11)	0.60 (0.10)	0.61 (0.09)	0.61 (0.09)	0.61 (0.08)
WHR	0.89 (0.08)	0.87 (0.08)	0.88 (0.08)	0.90 (0.08)	0.91 (0.08)	0.91 (0.07)
Obesity, n (%)						
Defined by BMI						
Yes	2013 (55%)	260 (63%)	502 (57%)	588 (59%)	498 (53%)	165 (41%)
No	1621 (45%)	155 (37%)	382 (43%)	406 (41%)	443 (47%)	235 (59%)
Defined by WC						
Yes	2484 (68%)	266 (64%)	572 (65%)	710 (71%)	661 (70%)	275 (69%)
No	1150 (32%)	149 (36%)	312 (35%)	284 (29%)	280 (30%)	125 (31%)
Defined by WHtR						
Yes	3297 (91%)	356 (86%)	775 (88%)	910 (92%)	882 (94%)	374 (94%)
No	337 (9%)	59 (14%)	109 (12%)	84 (8%)	59 (6%)	26 (7%)
Defined by WHR						
Yes	2336 (64%)	201 (48%)	480 (54%)	664 (67%)	678 (72%)	313 (78%)
No	1298 (36%)	214 (52%)	404 (46%)	330 (33%)	263 (28%)	87 (22%)

*denotes data collected at V1 were used. All other characteristics were based on data collected at V2.

SD=standard deviation; GED=General Educational Development; BMI=body mass index; WC=waist circumference; WHtR=waist-to-height ratio; WHR=waist-to-hip ratio.

Table 2. Cross-sectional Analysis of Standardized Anthropometric Measures at V2 by Age Group

	Age (years)					
Anthropometric Measures	**25-<45 (Ref)** β (95% CI)*	**45-<55** β (95% CI)	**55-<65** β (95% CI)	**65-<75** β (95% CI)	**75+** β (95% CI)	**p-value for trend**
BMI	0	-0.25 (-0.37, -0.14)	-0.31 (-0.42, -0.20)	-0.48 (-0.60, -0.36)	-0.80 (-0.94, -0.66)	<.0001
WC	0	-0.12 (-0.24, -0.00)	-0.01 (-0.12, 0.11)	-0.09 (-0.21, 0.03)	-0.27 (-0.41, -0.13)	0.018
WHtR	0	-0.12 (-0.24, -0.01)	-0.0 1(-0.12, 0.11)	-0.05 (-0.17, 0.07)	-0.18 (-0.32, -0.03)	0.325
WHR	0	0.08 (-0.03, 0.20)	0.35 (0.23, 0.46)	0.43 (0.31, 0.55)	0.48 (0.33, 0.62)	<.0001

*β coefficient and 95% confidence interval (CI) from linear regression models, adjusting for sex, education, physical activity, smoking status, alcohol consumption, and nutritional intake.

BMI=body mass index; WC=waist circumference; WHtR=waist-to-height ratio; WHR=waist-to-hip ratio; CI: Confidence Interval; Ref: reference group.

adjusted mean WHR was close to half SD unit higher in the oldest age group than in the youngest age group (β (95% CI) 0.48(0.33,0.62)). The tests for trend for BMI, WC and WHR were statistically significant ($p<.05$). No statistically significant sex*age interactions were observed (Supplemental Table 1).

Longitudinal analysis

Figure 1 depicts the anthropometric data for longitudinal analysis by sex and age group (< 45, 45-< 55, 55-< 65, 65-< 75, and 75+ years at V2). The mean anthropometric measures of obesity at V2 and V3 were calculated and plotted against the mean age at the respective visits. As shown in Figure 1, the mean BMI and WHtR were higher in women than in men, while the mean WC and WHR were lower in women than in men across time and in all age groups.

Figure 2 shows the results of changes in standardized anthropometric measures of obesity per every 5 years increase in age (aging) from mixed effects models adjusting for covariates, by sex and age group. A positive coefficient (*i.e.*, on the right side of the vertical reference line at '0') indicates an increasing trend with aging and a negative coefficient indicates a decreasing trend with aging. As shown in Figures 2a-2c, aging was associated with increased BMI, WC, and WHtR among younger age groups, but the increasing trend tended to be diminished or reversed among older age groups in both sexes. For example, for BMI, 5 year aging was associated with increase of 0.13 (0.06, 0.20) SD units in BMI in age groups 25-< 45 and 0.09 (0.05, 0.14) SD units in 45-< 55 years , but the trend reversed in age groups 65 years or older with decrease of -0.07 (-0.10, -0.03) SD units in age group of 65-< 75 years, and -0.14 (-0.19, -0.09) SD units in 75+ years among women (Figure 2a). On the other hand, WHR tended to increase with aging across all sex and age groups, although the magnitude of the increasing trend generally decreased in older age groups (Figure 2d). For instance, with each 5-year of aging, the mean WHR increased by 0.74 (0.52, 0.97) SD units for 25-< 45 years, 0.51 (0.39, 0.62) SD units for 45-< 55 years, 0.50 (0.38, 0.62) SD units for 55-< 65 years, 0.47 (0.34, 0.59) SD units for 65-< 75 years, and 0.24 (0.05, 0.44) SD units for 75+ years among male. Additionally, WHR had the highest SD unit increase with aging among the four anthropometric measures of obesity examined. For instance, among men 45 years and younger, the mean WHR increased by 0.74 (95% CI 0.52, 0.97) SD unit with each 5-year of aging, while the mean BMI, WC, and WHtR increased only by 0.14 (0.05, 0.23), 0.28 (0.16, 0.40), and 0.30 (0.17, 0.42) SD unit, respectively. Statistically significant sex*age interactions were observed in the analysis for WHR among 25-< 45 years group and WC among 45-< 55 years group (Supplemental Table 2) although they were in the same direction, but different magnitudes of the increasing trend among different sexes (Figure 2).

DISCUSSION

In this study of a large sample of adult AA men and women in Jackson, MS, we found that in cross-sectional analyses, compared to the younger age group, the older age group had a lower mean BMI, WC, and WHtR, but a higher mean WHR. In longitudinal analyses, the effect of aging on the changes in BMI, WC, and WHtR was similar; with the mean values increasing with age only among younger groups. In contrast, the mean WHR increased with age across all age groups.

The observation that BMI, WC and WHtR decreased with age while WHR increased with age in the older age group suggests that loss of lean muscle mass or change in the distribution of fat and lean mass with age may play an important role in disease risks associated with obesity in older adults. This may also partially explain why older adults considered to be overweight based on BMI have a lower mortality rate than those with lower BMI (the "obesity paradox") [27]. In a prospective cohort study among male health professionals in the US, a significant positive monotonic association between predicted fat mass and all-cause mortality, and a U-shaped association between predicted lean body mass and all-cause mortality were found, suggesting that the "obesity paradox" may be largely caused by low lean body mass, instead of low-fat mass, in the lower BMI range [28]. In another prospective cohort study of older British men, it was found that sarcopenia and central adiposity were associated with higher all-cause mortality [29]. In our own analyses in the JHS, we found the relationships between BMI, WC, WHtR and overall mortality to be J-shaped whereas there was a monotonic increasing relationship between WHR and overall mortality, suggesting once corrected for gluteal muscle mass, lower BMI or central adiposity does not afford greater mortality risks [30]. Aging is related to muscle loss and visceral fat accumulation, and has been associated with several cardio-metabolic chronic diseases and mortality [31]. Therefore, anthropometric measures and aging are together key risk factors of chronic diseases and mortality. This analyses further reveal the relationship between the two risk factors, and explains the rationale behind the relationships among risk factors and mortality in AA adults. These findings with WHR fit well with the postulated biological changes in old age, including redistribution of adiposity from limbs to visceral with concomitant loss of lean muscle mass, as approximated by waist circumference (central adiposity) and hip circumferences (gluteal muscle), respectively [23]. Therefore, WHR has been reported to be a better predictor of obesity-related risk among older adults than BMI and WC [32, 33].

Reviewers of an earlier version of this manuscript suggested that we include comorbid conditions as covariates in our analysis. We have opted not to adjust for comorbidity because comorbidity, in our opinion, does not meet the definition of confounder as it does not cause or prevent obesity. Rather, comorbidity may be caused in part by old age/aging (the exposure) and is also correlated with obesity, thus adjusting for it may introduce bias [34]. Furthermore, given that our objective is to describe the variation of obesity with age and possibly identify a better measure to monitor obesity (*i.e.*, not to explain it), adjusting for morbidity associated with obesity that may potentially mask the relationship between age and obesity would seem to defeat our purpose.

The strengths of this study include the large sample size and longitudinal follow-up of a well-characterized cohort of adult AAs, including a substantial proportion of elderly men and women with anthropometric measures of obesity across two visits, and a relatively high retention rate (86%) across visits. However, this study has several limitations. First, the longitudinal change in anthropometric measures over the life-course were derived from participants from different birth cohorts. While it is reasonable to assume that the longitudinal trend observed in anthropometric measures may be consistent with the biology of aging irrespective of birth cohort, we cannot be certain without longer term follow-up of participants of the same birth cohort. Furthermore, the anthropometric measures from V2 and V3 were used for the analysis, while the covariates including education, physical activity, smoking status, alcohol consumption, and nutritional intake collected at V1 were used for the analysis since they were not collected at V2. In addition, the results may not be generalizable to all AA adults across the US, as the sample was drawn solely from residents of Jackson, MS.

CONCLUSION

Our results showed that among middle age AA adults, all four anthropometric measures of obesity examined (BMI, WC, WHtR, and WHR) increased with aging. However, among elderly AA adults, WHR was the only anthropometric measures that showed continued increase with aging. Our findings suggest that WHR, a measure that captures both central adiposity and body composition, may be an important anthropometric measure to collect to monitor obesity and obesity-related health risks among older AA adults. These findings should be verified in other ethnically diverse populations.

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DISCLAIMER

The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the National Heart, Lung, and Blood Institute; the National Institute for Minority Health and Health Disparities; the National Institutes of Health; or the U.S. Department of Health and Human Services.

AUTHORS' CONTRIBUTIONS

YG–analysis and interpretation of data, drafting and final approval of the manuscript; YM–statistical expertise, helped conduct the literature review, critical review and final approval of the manuscript; RAB– critical review and final approval of the manuscript; AGB– critical review and final approval of the manuscript; AC–conception and design of study, critical review and final approval of manuscript. All authors have read and approved the manuscript.

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Department of Health (HHSN268201800015I) and the University of Mississippi Medical Center (HHSN268201800010I, HHSN268201800011I and HHSN268201800012I).

AVAILABILITY OF DATA AND MATERIALS

As a National Heart, Lung, and Blood Institute (NHLBI)-funded study, the JHS follows the NHLBI's policy for data sharing, which includes depositing the data into the NHLBI's Biologic Specimen and Data Repository Information Coordinating Center (BioLINCC) to make it publicly available to other investigators. The link to the JHS dataset: https://biolincc.nhlbi.nih.gov/studies/jhs/. Download directions are provided on the website. NHLBI further requires the JHS to maintain the accuracy of this dataset, so the JHS Coordinating Center sends modifications to BioLINCC for incorporation as appropriate. Privacy and access settings are controlled by BioLINCC, and the investigators have no influence on these settings.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study was approved by the Institutional Review Board of the University of Mississippi Medical Center (UMMC IRB Tracking Number: 1998-6004; DHHS FWA: 00003630 0000043; IORG: 00000061; IRB Registration: 00005033) and participants provided written informed consent. The JHS is an observational cohort study. No experiments were performed in the study.

PATIENT CONSENT FOR PUBLICATION

Not applicable.

COMPETING INTERESTS

None.

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Legend/caption for Figures

Figure 1's title: Figure 1(a)-(d). Mean anthropometric measures values at V2 to V3 by age-group and sex.

Figure 1's brief explanation: Each line shows the changes of unadjusted mean anthropometric measure from V2 to V3 for each age group stratified by sex.

yrs=years.

Figure 2's title: Figure 2(a)-(d). Longitudinal analyses of changes of standardized anthropometric measures per 5-year aging by sex and age group.

Figure 2's brief explanation: Mixed effects models with random intercept and random slope were used to test aging effect. Models were adjusted for covariates collected at V1, including age, education, physical activity, smoking status, alcohol consumption, and nutritional intake.

M=male; F=female; yrs=years; CI=Confidence Interval.

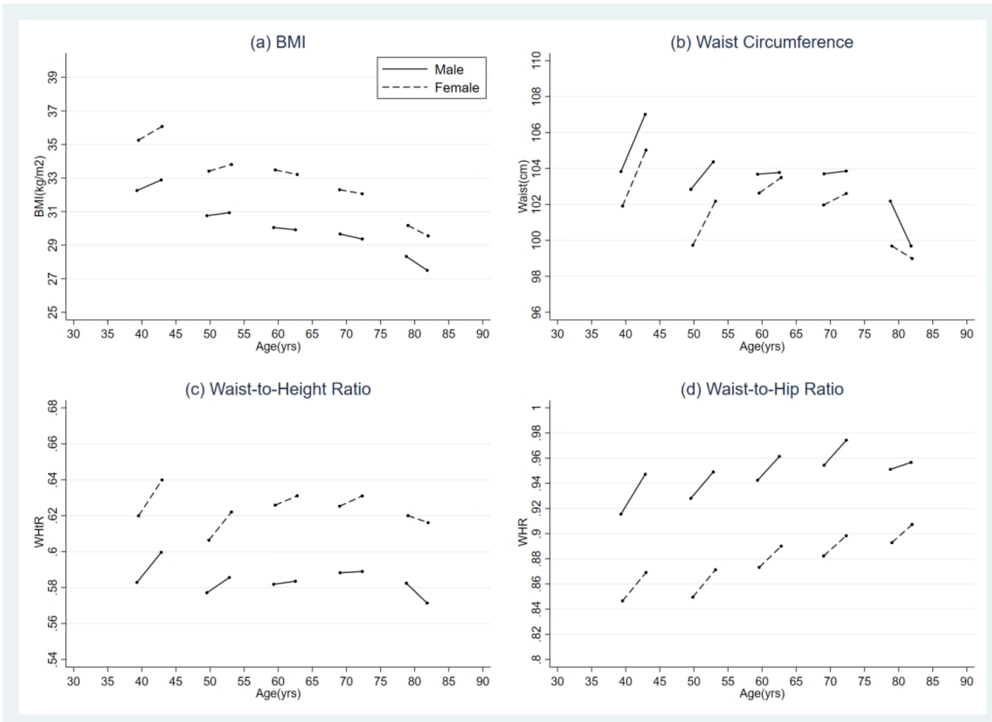

Figure 1(a)-(d). Mean anthropometric measures values at V2 to V3 by age-group and sex.
Each line shows the changes of unadjusted mean anthropometric measure from V2 to V3 for each age group stratified by sex.
yrs=years.

512x372mm (96 x 96 DPI)

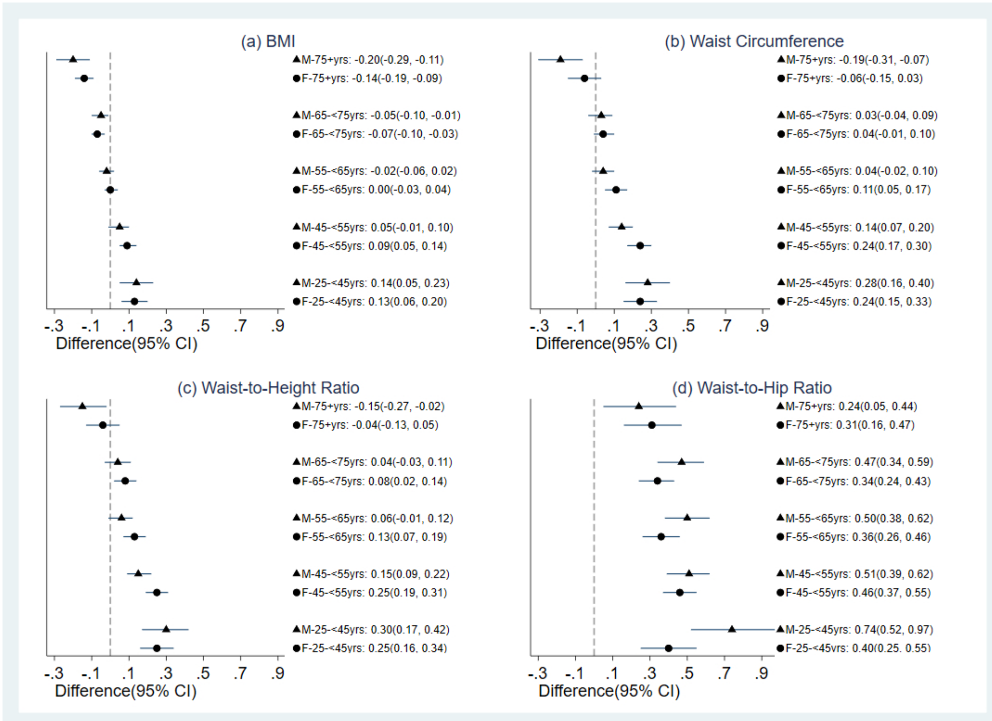

Figure 2(a)-(d). Longitudinal analyses of changes of standardized anthropometric measures per 5-year aging by sex and age group.
Mixed effects models with random intercept and random slope were used to test aging effect. Models were adjusted for covariates collected at V1, including age, education, physical activity, smoking status, alcohol consumption, and nutritional intake.
M=male; F=female; yrs=years; CI=Confidence Interval.

190x138mm (144 x 144 DPI)

Supplemental Table 1. P-values for effect modification by sex on the associations between obesity measures and age group in cross-sectionally analysis.

Anthropometric Measures	P-value for effect modification by sex
BMI	0.917
WC	0.869
WHtR	0.815
WHR	0.691

The sex*age group interaction term was included in linear regression models adjusting for sex, education, physical activity, smoking status, alcohol consumption, and nutritional intake.
BMI=body mass index; WC=waist circumference; WHtR=waist-to-height ratio; WHR=waist-to-hip ratio.

Supplemental Table 2. P-values for effect modification by sex on the associations between obesity measures and aging in each age group in longitudinal analysis.

Anthropometric Measures	25-<45 yrs.	45-<55 yrs.	55-<65 yrs.	65-<75 yrs.	75+ yrs.
BMI	0.929	0.160	0.475	0.726	0.281
WC	0.657	0.050	0.157	0.792	0.100
WHtR	0.604	0.051	0.139	0.418	0.187
WHR	0.007	0.534	0.082	0.119	0.602

The sex*follow-up time interaction term was included in mixed effects models with random intercept and random slope were used to test aging effect. Models were adjusted for covariates including education, physical activity, smoking status, alcohol consumption, and nutritional intake.
BMI=body mass index; WC=waist circumference; WHtR=waist-to-height ratio; WHR=waist-to-hip ratio; yrs.= years.

STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*

Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1-2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2-3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	3	State specific objectives, including any pre-specified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	6
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	n/a
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6-8
Bias	9	Describe any efforts to address potential sources of bias	n/a
Study size	10	Explain how the study size was arrived at	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7-8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	9
		(*b*) Describe any methods used to examine subgroups and interactions	9
		(*c*) Explain how missing data were addressed	n/a
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed	n/a

		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	n/a
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6
		(b) Give reasons for non-participation at each stage	n/a
		(c) Consider use of a flow diagram	n/a
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	10
		(b) Indicate number of participants with missing data for each variable of interest	n/a
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	n/a
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	n/a
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	n/a
		Cross-sectional study—Report numbers of outcome events or summary measures	11-15
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	11-16
		(*b*) Report category boundaries when continuous variables were categorized	n/a
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	n/a
Discussion			
Key results	18	Summarise key results with reference to study objectives	16-17
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	18
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	16-18
Generalisability	21	Discuss the generalisability (external validity) of the study results	18
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	19

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.