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Associations between obesity class and ambulatory blood pressure curves in African American women

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Abstract

Objective: Studies of body size and blood pressure (BP) in African American women typically focus on obesity overall or collapse obesity classes II and III into a single subgroup, ignoring potential heterogeneity in associations across categories. Moreover, ambulatory BP outcomes are primarily analyzed as mean daytime and/or nighttime BP, without examination of circadian changes during the day-to-night transition or the full 24-h cycle.

Methods: Functional data analysis methods were used to examine whether obesity categories modified ambulatory monitoring-assessed BP circadian rhythm in a cohort of 407 African American women.

Results: Age-adjusted systolic BP (SBP) was 4 mm Hg (95% CI: 0.4–8.4) higher among women with class I or II obesity than those with normal weight or overweight from 12:30 p.m. through 8:00 a.m. Age-adjusted differences in SBP among women with class III obesity versus those with normal weight or overweight were 6 mm Hg (95% CI: 0.7–10.8) during daytime hours and increased to 11 mm Hg (95% CI: 5.8–16.0) overnight. Compared with all other BMI categories, SBP of women with class III obesity declined more slowly from day to night.

Conclusions: Circadian BP among African American women was distinct among those with class III obesity compared with those with other body weight categories, suggesting that intervention efforts in African American women should target this group.

INTRODUCTION

Data show that African American women in the United States have among the highest rates of obesity (body mass index [BMI] ≥ 30 kg/m^2) globally [1]. Findings from the National Health and Nutrition Examination Survey (NHANES) show that obesity rates are highest in African American women compared with other race-sex groups in the United States, with 2017–2018 rates of 57% compared with 40% in White women, 41% in African American men, and 45% in White men [2]. Furthermore, class I (i.e., 30 kg/m^2 ≤ BMI < 35 kg/m^2), class II (i.e., 35 kg/m^2 ≤ BMI < 40 kg/m^2), and class III obesity (i.e., BMI ≥ 40 kg/m^2) have trended upward in African American women for several decades [1]. Obesity is a significant driver of excess rates of elevated blood pressure (BP) and hypertension, which have been linked to adverse outcomes such as heart disease and stroke, with especially pronounced associations among African American individuals [3,4].

Most studies that have examined associations between BMI and BP or other health outcomes have collapsed the higher BMI categories, which may obscure differences among obesity classes [5–9]. A notable exception, findings from the UK Biobank study of predominately (93%) White adults demonstrated that, in comparison with class I obesity, class III obesity was associated with increased risk for adverse cardiovascular events with or without the presence of hypertension, hypercholesterolemia, and diabetes, whereas class II obesity was only associated with increased risk when at least one additional risk factor was present [10]. Such findings have important implications for clinical guidelines and recommendations, which often assume comparable levels of disease vulnerability in people with obesity regardless of obesity class. Distinctions across obesity classes may be especially relevant for African American women, who have the highest prevalence of class II and class III obesity compared with other race-sex groups [1]. In particular, several authors have argued for increasing clinical BMI cut points for obesity in African American women. But these increases would only be to values of 31 to 33 kg/m^2, which is still in the class I obesity category [11,12]. To date, however, there is a remarkable lack of research on differences in BP or other clinical risk profiles for African American women across the subcategories of obesity. Because BP is an important precursor to later-life clinical events (e.g., stroke, heart disease), it represents a crucial target for early prevention efforts in this group.

The current study examines associations between BMI categories and BP in a cohort of African American women. Most prior studies of BMI and BP have primarily focused on categorical hypertension (systolic BP [SBP] ≥ 130 mm Hg or diastolic BP [DBP] ≥ 80 mm Hg) based on clinic measurements during the day [1,13,14]. However, BP has a circadian rhythm whereby it increases in the morning, remains relatively constant throughout the day, and decreases by at least 10% during nighttime [15]. Given this, we assessed BP via ambulatory BP monitoring (ABPM), which captures readings during daytime and nighttime, as well as the circadian BP curve, i.e., each BP measurement and its corresponding timing. Prior studies examining ABPM outcomes have typically focused on mean daytime or nighttime BP levels alone [7]. However, depending on the temporal pattern of an ABP curve, using means as observed BP levels can result in a loss of important biological information on circadian BP [16]. For example, a 2021 study showed that the shapes of ABP curves were significantly associated with cardiovascular outcomes where summary ABP parameters (i.e., dipping and morning surge) were not [17]. Our analytic approach uses methods from the growing subfield of methodological and theoretical statistics known as functional data analysis [18]. These methods allow retention of all within-person variability and simultaneously analyze daytime and nighttime BP levels and, thus, circadian BP. We hypothesized that, relative to African American women with normal weight or overweight, women with class II and class III obesity would have higher BP over a 24-h period, and women with class III obesity would exhibit the greatest circadian BP disruptions.

Study Importance

What is already known?

- Elevated blood pressure (BP) and obesity disproportionately impact African American women in the United States.
- Associations between obesity and BP may be heterogeneous across obesity classes and differ by the time of day at which BP is assessed (i.e., daytime or nighttime).

What does this study add?

- Overweight was not associated with elevated BP in early middle-aged African American women.
- Although overall obesity (class I, II, and III) was associated with elevated BP, only class III obesity was associated with disrupted circadian patterns (e.g., slowed decrease from day to night) of BP.

How might these results change the direction of research or the focus of clinical practice?

- Overweight, as defined by BMI, may have limited, if any, impact on BP among early middle-aged African American women.
- Interventions aimed to lower obesity-related risks of elevated BP among African American women should focus on those with class III obesity.

METHODS

Participants

The Mechanisms Underlying Stress and Emotions (MUSE) in African American Women's Health Study follows a cohort of premenopausal African American women with at least one intact ovary who were aged 30 to 45 years and living in or near Atlanta, Georgia, at prescreening. Eligible participants were identified through commercial residential lists and voter registration records from various Atlanta-area census tracts and were screened for cardiovascular disease, pregnancy/lactation, chronic illnesses which influence atherosclerosis (e.g., autoimmune, inflammatory, renal, liver disease), psychiatric treatment, illicit drug use, alcohol abuse, and overnight shift work. Of those 831 individuals screened by phone, 422 completed in-person visits between December 2016 and March 2019 [19].

ABP data were missing for eight participants due to cuff size limits (three cases), equipment failure (three cases), and refusal (two cases).

Weight, and thus BMI, was missing for one participant. Six others lacked at least one covariate. Of the 422 MUSE participants, we examined data from $N = 407$ with nonmissing BMI, ABP, and covariates.

The study was approved by the Emory University institutional review board, with all participants providing oral and written informed consent.

ABPM

In this study, 48-h ABPM was conducted using the OnTrak model 90227 (Spacelabs Healthcare). A participant's ABPM count is the number of ABP readings obtained. The study protocol intended readings every 30 min during daytime (8 a.m. to 9:59 p.m.) and every hour during nighttime (10 p.m. to 7:59 a.m.) for an intended ABPM count of 76. Daytime SBP (DT SBP) and nighttime SBP (NT SBP) are mean SBP during daytime and nighttime, respectively, with DT DBP and NT DBP defined similarly. Online Supporting Information Supplement A summarizes ABPM characteristics, including intervals between readings.

BMI

Height and weight were measured in person and used to calculate BMI, categorized by the following US Centers for Disease Control and Prevention (CDC) guidelines [20]: underweight (BMI < 18.5 kg/m^2); normal weight (18.5 kg/m^2 ≤ BMI < 25 kg/m^2); overweight (25 kg/m^2 ≤ BMI < 30 kg/m^2); class I obesity (30 kg/m^2 ≤ BMI < 35 kg/m^2); class II obesity (35 kg/m^2 ≤ BMI < 40 kg/m^2); and class III obesity (BMI ≥ 40 kg/m^2). Analyses conducted with all groups revealed no BP differences between women with normal weight and overweight or between women with class I and class II obesity (online Supporting Information Supplement B). Therefore, we proceeded with the following consolidated categories: 1) normal weight and overweight; 2) class I and class II obesity; and 3) class III obesity. One participant with underweight (BMI = 17.16 kg/m^2) was categorized as having normal weight.

Covariates

Covariates were potential confounders shown to be associated with BMI and ABP in previous research. Covariates representing socioeconomic status were highest education level attained, employment status, marital/partnership status, and annual household income and household size (i.e., number of people living in the same household as the participant; used to adjust for income) [21–23]. Clinical and behavioral covariates included age, current cigarette smoking status, self-reported antihypertensive medication use (without regard to type), parity, and intentional exercise (based on typical time spent performing activities such as weight lifting and walking for exercise in metabolic equivalents of task [MET-hours per week]) [24–27]. Diabetes was not included because only 17 (4.2%) participants reported having it.

Statistical methods

Descriptive statistics were computed for DT and NT SBP, ABPM count, adequate ABPM, and all covariates. Categorical variables were summarized with counts and percentages. Continuous variables with symmetric histograms were summarized with means and standard deviations (SD); those with nonsymmetric histograms were summarized with quartiles. Covariates were examined for associations with BMI using χ^2 tests for categorical variables, ANOVA for symmetric continuous variables, and Kruskal–Wallis tests for nonsymmetric continuous variables. Tukey adjustment for multiple comparisons was used in post hoc, pairwise comparisons.

Associations of BMI with DT and NT BP were analyzed using multiple linear regression controlling for age first and subsequently for all covariates.

Functional data analysis

Generalized additive mixed models (GAMMs) [28] were used to estimate average 24-h ABP curves for each BMI category. The simplest form of GAMMs for ABP (ignoring BMI and covariates) is akin to a mixed-effects regression model, with time as a nonlinear fixed effect and participant-specific random intercepts. The model estimates a "smooth" function of time constructed from a basis of cyclic cubic splines. Within-participant correlation is addressed by participant-specific random effects with autocorrelation-1 structure.

Associations of BMI with ABP curves were assessed in the following two models: age-adjusted and fully adjusted (i.e., all covariates). Both used the spline and correlation structures as described earlier. However, these models include ABP curves for each BMI class to account for the relationships between BMI class and ABP over time, as well as class-specific intercepts accounting for the time-invariant relationship between BMI class and ABP.

These models examine heterogeneity in the relationship between time and ABP across BMI classes, extending the concept of regression with an interaction between BMI and time to a nonlinear setting. Uncertainty in the estimated curves and their differences was quantified with 95% simultaneous confidence bands produced by 10,000 simulations, which account for multiple comparisons across time points [29].

Although ABPM occurred over 48 h, data were modeled as 24-h ABP curves, with the time variable t assigned to have a value of $t = 0$ at 8 a.m. on each day of ABPM. The times of other BP readings are assigned values of $0 < t < 1$. Analyses were conducted on SBP and DBP separately, using all available data, and then were compared with analyses in restricted samples (see *Results*). This report focuses on analyses of SBP because DBP was not associated with BMI (online Supporting Information Supplement C).

Sensitivity analyses

Sensitivity analyses restricted data to participants who met the following criteria: 1) had adequate ABPM; and/or 2) were not taking antihypertensive medications.

Statistical analyses were conducted and plots were produced using R version 4.2.3 (R Project for Statistical Computing). The type I error rate of $\alpha = 0.05$ was used to indicate statistical significance. GAMMs were fit using *mgcv* [30]. Simultaneous confidence bands and plots were created with *itsadug* [31].

RESULTS

Descriptive statistics

BMI was distributed as 43.9% of participants with normal weight or overweight, 38.7% with class I or II obesity, and 17.4% with class III obesity. At 56.1%, most participants had obesity. SBP was associated with BMI class (Table 1), with mean DT SBP of women with class III obesity being 3.9 mm Hg higher than those with normal weight or overweight and 2.3 mm Hg higher than those with class I or II obesity. Nighttime differences were 7.8 mm Hg and 3.2 mm Hg, respectively. Table 1 shows that higher BMI was associated with higher household sizes, higher proportions of antihypertensive medication, lower proportions of college graduates, and lower proportions of adequate ABPM.

For descriptive purposes, Figure 1 displays observed and estimated ABP among MUSE participants, with colors corresponding to BMI class. Estimated curves were not adjusted for covariates and were fit separately within each group.

BMI and mean SBP

Tables 2 and 3 display age-adjusted estimated marginal means of DT and NT SBP, respectively. In Table 2, age-adjusted DT SBP was 118.8 mm Hg (95% confidence interval [CI]: 117.0–120.6) among women with normal weight or overweight, 122.7 mm Hg (95% CI: 120.8–124.6) among those with class I or II obesity, and 125.2 mm Hg (95% CI: 122.4–128.0) among those with class III obesity. DT SBP of women with class III obesity was 6.4 mm Hg (95% CI: 3.0–9.7) higher than those with normal weight or overweight ($p < 0.01$). Similarly, DT SBP of women with class I or class II obesity was 3.9 mm Hg (95% CI: 1.3–6.5) higher than those with normal weight or overweight ($p = 0.01$). Table 3 shows that age-adjusted NT SBP was 108.2 mm Hg (95% CI: 105.8–110.6) among women with normal weight or overweight, 112.8 mm Hg (95% CI: 109.6, 115.9) among women with class I or II obesity, and 116.1 mm Hg (95% CI: 112.9–119.3) among women with class III obesity. These corresponded to 4.6-mm Hg (95% CI: 2.1–7.0, $p < 0.01$) and 7.9-mm Hg (95% CI: 4.7–11.0, $p < 0.01$) higher NT SBP among women with class I or class II obesity and women with class III obesity compared with those with normal weight or overweight, respectively.

Functional analysis of BMI and SBP

Figure 2A shows age-adjusted ABP curves for each BMI class. Among women with normal weight or overweight, DT SBP was ~119 mm Hg and NT SBP decreased to as low as 104 mm Hg. For women with class I or II obesity, DT SBP was ~122 mm Hg and NT SBP decreased to a minimum of 108 mm Hg. For women with class III obesity, DT SBP was ~125 mm Hg and NT SBP decreased to a minimum of 111 mm Hg. Notably, the low achieved among women with class III obesity occurred later (around 5 a.m.) than the low achieved for other groups (between 3 and 4 a.m.). Age-adjusted DT SBP estimates at specific times (Figure 2, Table 2) display relative stability, after the initial morning BP surge. On the other hand, age-adjusted NT SBP estimates (Figure 2, Table 3) exhibit the circadian dipping pattern associated with overnight BP. However, Figure 2 also exhibits a slower day-to-night decrease in BP among women with class III obesity, which is followed by a morning increase resembling that of women with class I or II obesity, i.e., a disruption to circadian BP.

Table 2 also displays select, time-specific, age-adjusted differences in DT SBP between women with normal weight or overweight and others. SBP was 5.7 to 6.7 mm Hg higher among women with class III obesity and 2.9 to 4.5 mm Hg higher among those with class I or II obesity than women with normal weight or overweight, respectively, between 8 a.m. and 8 p.m. The magnitudes of these differences remained stable throughout daytime hours and reflect differences observed in DT SBP. However, nighttime differences show more variability over time (Table 3) and diverge from differences found in NT SBP. SBP for women with class III obesity was 5.7 to 10.9 mm Hg higher than those with normal weight or overweight. Differences in SBP between women with class I or class II obesity and those with normal weight or overweight were relatively stable overnight at 3.7 to 4.6 mm Hg. Figure 2B–D provide a visualization of the differences among groups over the 24-h time course. It shows that women with class III obesity had higher SBP than women with normal weight or overweight during the entire time course, controlling for age, whereas their SBP was higher than women with class I or II obesity during the period of 11 p.m. to 3:30 a.m. SBP among women with class I or class II obesity was mean (SE) 4.9 (2.01) mm Hg higher than among women with normal weight or overweight (Figure 2) at all times except for 8 a.m. to 12:30 p.m. and 10:30 p.m. to 12 a.m.

Time-specific differences among groups were also significant in the fully adjusted model, with reduced magnitude and shorter time intervals in some cases (online Supporting Information Supplement D). In the fully adjusted model, women with class III obesity presented mean (SE) SBP that was 5.1 (2.66) mm Hg to 8.5 (2.66) mm Hg higher than those with normal weight or overweight from 8:30 p.m. until 4:30 a.m., instead of the entire time course, as seen in the age-adjusted model. Differences between women with class III obesity and women with class I or II obesity occurred between 11:30 p.m. and 12:30 a.m. in the fully adjusted model, instead of 11 p.m. and 3:30 a.m. as seen in the age-adjusted model, with magnitudes around 5.2 (2.64) mm Hg. The difference between women with class I or II obesity and women with normal weight or overweight remained stable at 2.7 (1.25) mm Hg.

TABLE 1 Summary statistics for selected variables, stratified by BMI class, among African American women in the Atlanta, Georgia, metropolitan area aged 30 to 46 years between 2016 and 2019.

	Total (*N* = 407)	Normal weight or overweight, BMI < 30 (*n* = 178)	Obesity class 1 or 2, 30 ≤ BMI < 40 (*n* = 158)	Obesity class 3, BMI ≥ 40 (*n* = 71)	*p* value
Mean (SD)					
Age	37.9 (4.26)	38.0 (4.38)	38.0 (4.22)	37.5 (4.07)	0.684
Arm circumference, cm	32.56 (5.39)	29.15 (3.99)[a]	33.85 (4.14)[b]	37.99 (5.03)[c]	<0.001
Clinic SBP, mm Hg	119.0 (14.67)	115.4 (12.98)[a]	121.4 (14.39)[b]	122.8 (17.22)[c]	<0.001
DT SBP, mm Hg	121.4 (12.31)	118.8 (11.77)[a]	122.7 (12.14)[b]	125.0 (12.79)[c]	<0.001
NT SBP, mm Hg	111.3 (11.70)	108.2 (10.46)[a]	112.8 (10.96)[b]	116.0 (14.09)[b]	<0.001
Median (25th percentile, 75th percentile)					
Intentional exercise, metabolic equivalents of task, MET-h/wk	29.0 (10.0, 60.5)	35.2 (14.0, 65.5)[a]	26.0 (9.9, 57)[a]	17.2 (7.2, 49.5)[a]	0.020
Household size	3.0 (2.0, 5.0)	3.0 (2.0, 4.75)[a]	3.0 (2.2, 4.8)[a]	4.0 (3.0, 5.0)[b]	0.024
Births given	2.0 (0.0, 3.0)	1.0 (0.0, 2.0)	2.0 (1.0, 3.0)	2.0 (1.0, 3.0)	0.068
ABPM count	73.0 (67.0, 76.0)	74.0 (71.0, 77.0)[a]	73.0 (68.0, 76.0)[b]	67.0 (58.0, 73.0)[c]	<0.001
n (%)					
Current smoking	42 (10.3)	19 (10.7)	19 (12.0)	4 (5.6)	0.332
Antihypertension medication	69 (17.0)	12 (6.7)[a]	31 (19.6)[b]	26 (36.6)[c]	<0.001
Employment					0.709
Unemployed	56 (13.8)	20 (11.2)	22 (13.9)	14 (19.7)	
Part-time	80 (19.7)	36 (20.2)	32 (20.3)	12 (16.9)	
Full-time	262 (64.4)	119 (66.9)	100 (63.3)	43 (60.6)	
Other	9 (2.2)	3 (1.7)	4 (2.5)	2 (2.8)	
Education level					0.030
0: High school or less	128 (31.4)	43 (24.2)	55 (34.8)	30 (42.3)	
1: Postsecondary	86 (21.1)	37 (20.8)	36 (22.8)	13 (18.3)	
2: College or higher	193 (47.4)	98 (55.1)[a]	67 (42.4)[b]	28 (39.4)[c]	
Income					0.174
<$35k	100 (24.6)	34 (19.1)	43 (27.2)	23 (32.4)	
$35k–$50k	85 (20.9)	37 (20.8)	33 (20.9)	15 (21.1)	
$50k–$75k	91 (22.4)	45 (25.3)	31 (19.6)	15 (21.1)	
>$75k	124 (30.5)	56 (31.5)	50 (31.6)	18 (25.4)	
Refused/do not know	7 (1.7)	6 (3.4)	1 (0.6)	0 (0.0)	
Married/partnered	150 (36.9)	58 (32.6)	67 (42.4)	25 (35.2)	0.168
Adequate ABPM	372 (91.4)	173 (97.2)[a]	141 (89.2)[b]	58 (81.7)[c]	<0.001

Note: Different superscripts (i.e., a, b, or c) indicate statistically significant differences in post hoc, pairwise comparisons of means. Matching superscripts indicate no statistically significant differences in post hoc, pairwise comparisons of means.
Abbreviations: ABPM, ambulatory blood pressure monitoring; DT, daytime; NT, nighttime; SBP, systolic blood pressure.

Sensitivity analyses

Sensitivity analyses examined the effect of BMI class in restricted samples. Findings in the sample restricted to adequate ABPM reflected those in the overall sample (online Supporting Information Supplement E.1), although adequate ABPM was less likely among those with higher BMI values ($p < 0.001$; Table 1). Results were also similar when data were restricted to the 338 women who did not take antihypertensive medications (Supplement E.2) and the 297 who were under both restrictions (Supplement E.3).

DISCUSSION

We examined circadian BP across BMI categories in a cohort of early middle-aged African American women representing a range of body sizes. A major contribution of this study was the ability to detect BP circadian rhythm among women with class III obesity compared with women in other BMI categories. This was enabled by the ability to retain this subgroup as distinct in contrast to prior studies that have often combined class III with class II and/or class I obesity [5–9].

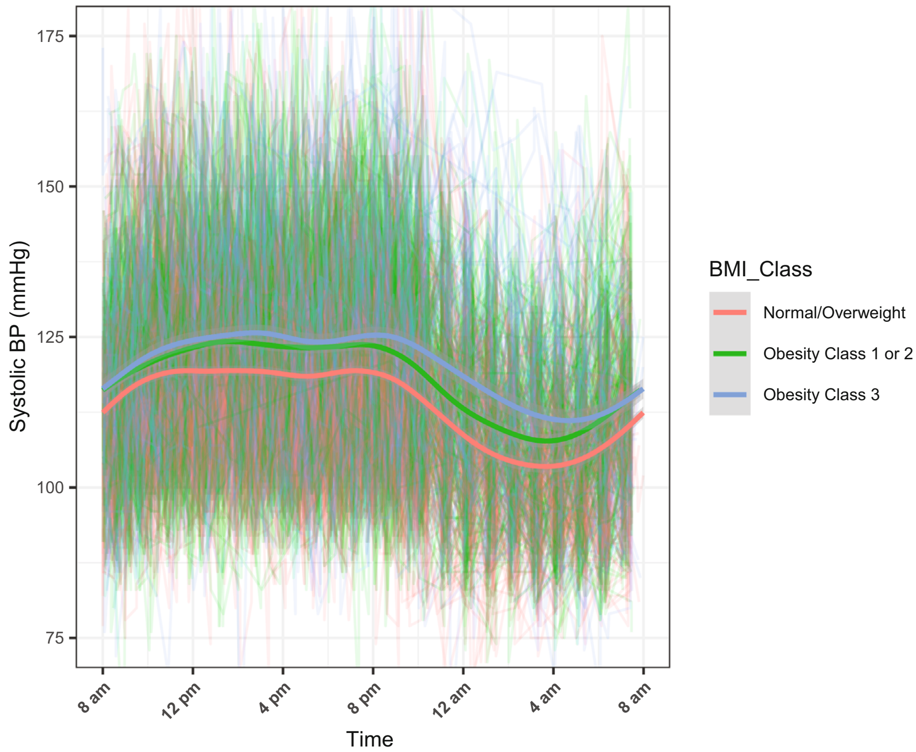

FIGURE 1 Observed and estimated ambulatory BP profiles by BMI class among African American women aged 30 to 46 years living in and around Atlanta, Georgia, during 2016 through 2019. Estimated profiles, depicted as smooth curves with (pointwise) 95% confidence bands in gray, were not adjusted for any covariates. BP, blood pressure. [Color figure can be viewed at wileyonlinelibrary.com]

TABLE 2 Mean age-adjusted DT SBP of African American women in the Atlanta, Georgia, metropolitan area at the average age of MUSE participants during the years 2016 through 2019 by BMI, overall (using mean ABP) and at specific times of day (using ABP profiles).

	OLS-fitted DT SBP, mm Hg	GAMM-fitted time-specific SBP, mm Hg			
BMI class	**8:00 a.m. to 9:59 p.m.**	**8:00 a.m.**	**12:00 p.m.**	**5:00 p.m.**	**8:00 p.m.**
Fitted mean (SE)					
Normal and overweight	118.8 (0.90)	112.4 (1.56)	119.6 (1.5)	117.8 (1.52)	119.2 (1.52)
Obesity C1 and C2	122.7 (0.96)	116.4 (1.67)	122.9 (1.60)	122.4 (1.61)	123.8 (1.61)
Obesity C3	125.2 (1.43)	118.1 (2.49)	125.4 (2.4)	125.9 (2.4)	125.9 (2.40)
Difference (SE)					
Normal and overweight	Ref.	Ref.	Ref.	Ref.	Ref.
Obesity C1 and C2	3.9 (1.31)*	3.2 (2.06)	2.9 (1.98)	4.4 (1.99)*	4.5 (1.99)*
Obesity C3	6.4 (1.69)*	5.7 (2.56)*	5.8 (2.47)*	5.5 (2.48)*	6.7 (2.48)*

Note: Differences in DT and time-specific BP between women with obesity C1 and C2 and those with normal and overweight were around mean (SE) 4 (≈ 2) mm Hg and statistically significant. Times were chosen to illustrate how BP changes during DT. Maximum SBP for women with normal weight, overweight, and obesity C1 and C2 occurred around 12 p.m. Maximum SBP for women with obesity C3 occurred at 8 p.m., outside of DT hours (not shown).
Abbreviations: ABP, ambulatory blood pressure; BP, blood pressure; DT, daytime; C1, class 1; C2, class 2; C3, class 3; GAMM, generalized additive mixed model; MUSE, Mechanisms Underlying Stress and Emotions; OLS, ordinary least squares; SBP, systolic blood pressure.
*Two-sided $p < 0.05$.

Our analyses used state-of-the art statistical methodology to capture the curvilinear relationships between time and ABP while accounting for within-person variability and adjusting for meaningful covariates. Results of this functional data analysis approach revealed no differences in SBP between women with normal weight and those with overweight or between women with class I obesity and those with class II obesity. With these pairs collapsed, exploratory analyses revealed that obesity (without regard to class) was associated with higher BP throughout the day and night, but associations only varied over time for women with class III obesity. Specifically,

TABLE 3 Mean age-adjusted NT SBP of African American women in the Atlanta, Georgia, metropolitan area at the average age of MUSE participants during the years 2016 through 2019 by BMI, overall (using mean ABP) and at specific times of night (using ABP profiles).

	OLS-fitted NT SBP, mm Hg	GAMM-fitted time-specific SBP, mm Hg			
BMI class	10:00 p.m. to 7:59 a.m.	10:00 p.m.	1:00 a.m.	4:00 a.m.	7:00 a.m.
Fitted mean (SE)					
Normal weight and overweight	108.2 (0.85)	115.3 (1.54)	106.3 (1.58)	103.5 (1.58)	109.1 (1.58)
Obesity C1 and C2	112.8 (0.90)	119.8 (1.63)	111.0 (1.68)	107.6 (1.69)	113.9 (1.69)
Obesity C3	116.1 (1.35)	123.9 (2.43)	117.1 (2.51)	112.2 (2.52)	114.8 (2.52)
Difference (SE)					
Normal weight and overweight	Ref.	Ref.	Ref.	Ref.	Ref.
Obesity C1 and C2	4.6 (1.62)*	4.6 (2.02)*	4.5 (2.08)*	3.7 (2.09)*	4.1 (2.09)*
Obesity C3	7.9 (1.60)*	8.6 (2.51)*	10.9 (2.6)*	8.6 (2.61)*	5.7 (2.6)*

Note: NT SBP of women with obesity C3 did not significantly differ from that of women with obesity C1 and C2. However, time-specific differences in SBP between women with obesity C3 and those with obesity C1 and C2 were significant during NT hours of 11 p.m. to 3:30 a.m. Differences in NT and time-specific SBP between women with obesity C1 and C2 and those with normal weight and overweight were around mean (SE) 4.5 (1.2) mm Hg and 4.9 (2.0) mm Hg, respectively, and were statistically significant.

Abbreviations: ABP, ambulatory blood pressure; BP, blood pressure; C1, class 1; C2, class 2; C3, class 3; GAMM, generalized additive mixed model; MUSE, Mechanisms Underlying Stress and Emotions; NT, nighttime; OLS, ordinary least squares; SBP, systolic blood pressure.

*Two-sided $p < 0.05$.

compared to women with normal weight or overweight, SBP of women with class III obesity was around 6 mm Hg (95% CI: 0.7–10.8) higher throughout daytime hours and up to 11.0mm Hg (95% CI: 5.8–16.0) overnight in age-adjusted analyses. In contrast, SBP of women with class I or II obesity was 4 mm Hg (95% CI: 0.4–8.4) higher than that of women with normal weight or overweight, a difference that persisted over much of the 24-h period. Results also showed that SBP decreased more slowly at night only among women with class III obesity compared with those with normal weight or overweight, a novel discovery enabled by our analytic approach.

To our knowledge, this study is one of the first to examine distinct associations between class II and/or class III obesity and ABP in a US-based cohort. However, our findings are somewhat consistent with prior studies of overall obesity and ABP. For example, a previous study conducted in Poland sampled 128 men and women with obesity who underwent 24-h ABPM prior to bariatric surgery. Results indicated that patients with class III obesity had 4.5-mm Hg and 7-mm Hg higher DT SBP and NT SBP, respectively, compared with patients with class I or II obesity [32]. Similarly, in a study of 5950 men and women living in Israel who underwent ABPM at a physician's request, DT SBP and NT SBP of women with obesity were 5 mm Hg and 7 mm Hg higher, respectively, than levels of SBP in women with normal weight [33]. The current study extends these prior results by focusing on African American women and having a more expansive distribution of BMI. We report important, and, to our knowledge, yet to be documented, differences for African American women with class III obesity compared with those with normal weight or overweight. These results suggest disparate cardiovascular health risks across obesity classes. Specifically, they show that, in African American women, obesity may only be associated with BP dysregulation at the upper limits of BMI. Consequently, interventions aimed at lowering the obesity-related risks of elevated BP among African American women may need to focus on individuals with class III obesity.

Commonly, statistical analyses of ABP use mean values to measure BP. However, that approach discards BP changes within each individual and has the potential to obscure circadian rhythms. In our cohort, we analyzed ABP using the traditional approach with mean values as well as a functional data analytic approach. Both approaches revealed significant positive associations between BMI categories and SBP. However, the nighttime periods over which differences occurred and the frequency with which differences changed were only observed using a functional data approach. This is important because higher NT SBP in particular has been associated with adverse cardiovascular outcomes, independent of DT SBP [34,35]. Moreover, other work has shown that patterns of ABP curves predicted cardiovascular outcomes when ABP parameters did not [26]. Taking advantage of the rich temporal information in ABPM data may inform downstream interventions to lower BP at night or mitigate adverse cardiovascular outcomes resulting from elevated BP at night. For example, modifications to the timing of both pharmacological and nonpharmacological interventions (e.g., meal-eating) have been suggested as potentially beneficial in mitigating disruptions of circadian BP [15]. However, evidence of such interventions' efficacy is still mixed.

This study has several limitations. Although higher BMI is widely accepted as corresponding with increased risk for cardiovascular disease, it should be noted that BMI does not account for lean versus fat body mass [36]. Body fat (i.e., adiposity) has been shown as the operative component of BMI contributing to risk of cardiovascular morbidity [37]. Our analyses lack differentiation between adiposity and other contributors to BMI. Waist circumference, waist-hip ratio, and imaging-based measures of body composition have been shown to be better estimates of adiposity when compared to BMI

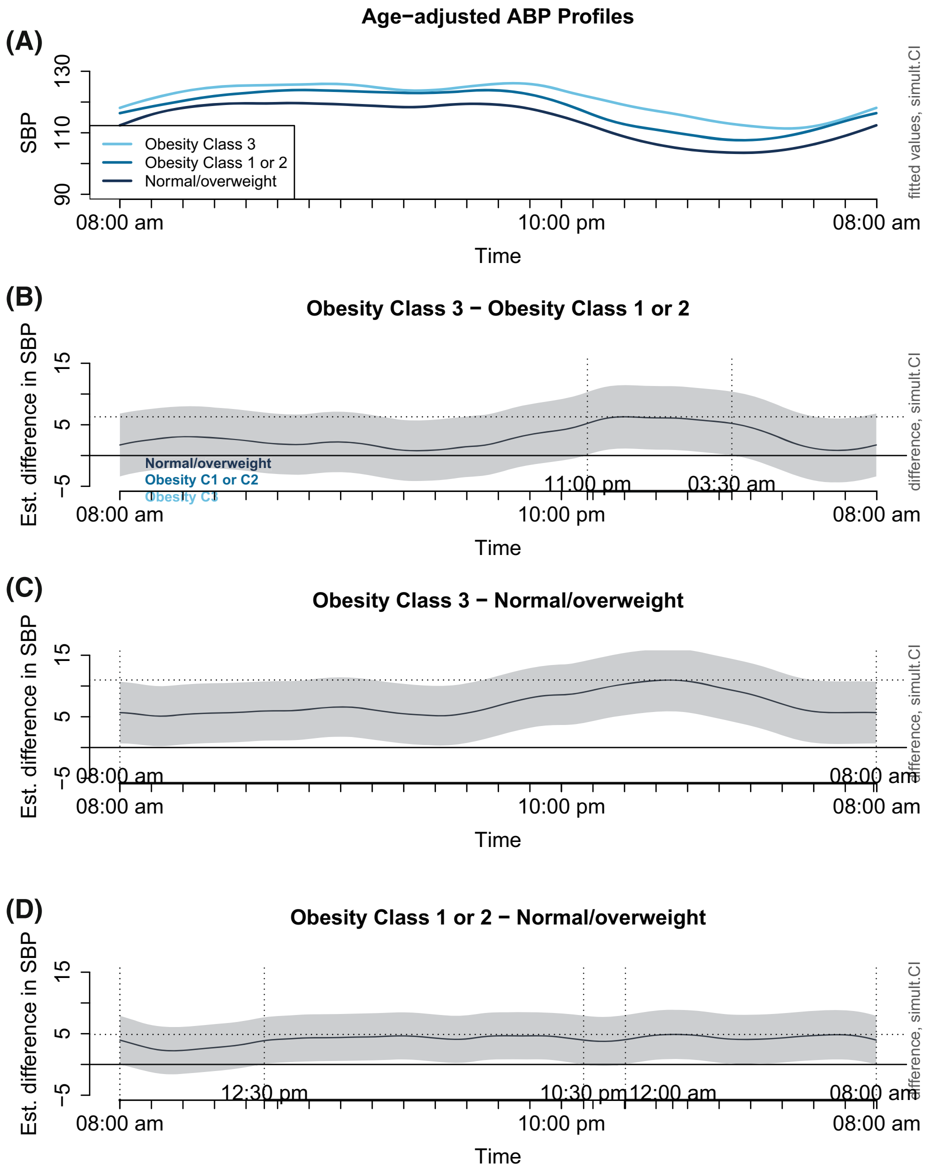

FIGURE 2 (A) Age-adjusted systolic ABP profiles for women with normal weight or overweight (light blue), class 1 or 2 obesity (blue), and class 3 obesity (dark blue). (B–D) Pairwise differences between profiles in panel A. Dotted vertical lines and times above the x-axis indicate statistically significant differences (i.e., 95% simultaneous confidence band does not contain zero) over the time interval represented by the accompanying bolded segment of the x-axis. Horizontal dotted lines show maximum difference. ABP, ambulatory blood pressure; C1, class 1; C2, class 2; C3, class 3; Est, estimated; SBP, systolic blood pressure. [Color figure can be viewed at wileyonlinelibrary.com]

[36,38,39]. However, the increased accuracy of adiposity measurement via waist circumference and waist-hip ratio may not hold for African American women, given the preponderance of data documenting less visceral fat among African American women compared with White women [40]. Another limitation is potential selection bias, as college-educated women were overrepresented (50% in our cohort vs. 25% of African American women nationally) [41]. However, in a cohort of African American women with lower socioeconomic status, we would have most likely had a higher proportion of women with obesity than in the current cohort, which would potentially increase the strength of our observed associations. Additionally, we cannot generalize to other race-sex groups because only African American women were enrolled in the MUSE Study. Similarly, these results may not be generalizable to the entire US population of African American women because they are from a specific geographical region and age range. However, it is important to note that this age range represents a critical period for BP increases in African American women's lives, as previous work has shown that cardiovascular events may occur at a lower threshold in women than in men, especially before age 52 years [42]. This study is also cross-sectional and lacks the temporality necessary to imply a causal relationship between BMI and BP. Finally, ABPM count was associated with BMI. Relatedly, mean arm circumference of women who did not undergo ABPM was larger, at mean (SD) 35.4 (10.72) in, than those who did, at 32.6 (5.55) in. However, among the eight women who did not undergo ABPM, five had normal weight, and three had class III obesity. Therefore, the smaller sample size among women with class III obesity is likely not solely attributable to difficulty wearing the ABPM device.

This study also has several strengths. We examined BP circadian rhythm across BMI categories in a disproportionately impacted population at a life stage (i.e., early middle age) when associations of SBP with cardiovascular risk may be exacerbated for women in comparison with similarly aged men [42]. A major contribution of this study was the ability to analyze individuals with class III obesity separately, in contrast to prior studies that have often combined class III obesity with other obesity subgroups [5–9]. Retaining class III obesity as a distinct subgroup allowed detection of the distinct BP circadian rhythm in this group compared with women with lower BMI values. To our knowledge, there have been no previous studies examining associations between obesity and ABP curves with a focus on class III obesity using a functional data analytic approach. Therefore, we present a novel exploration of time-dependent associations between BMI categories and ABP. Furthermore, few studies of ABP have included analyses of mean and functional ABP, allowing for both summaries and more nuanced views of differences among groups. Additionally, studying this cohort may confer more insights into issues related to cardiovascular health that are specific and pertinent to African American women.

MUSE is an ongoing study that continues to collect data related to cardiovascular risk. Future work will examine associations between important predictors (e.g., BMI, experiences of stress) and ABP longitudinally. Future research should also aim to develop more clinically meaningful measures of adiposity and cutoffs for African American women. Our focus on this population allows us to begin developing cutoffs for BMI or other risk factors that are more salient for this population compared with cutoffs developed from samples/cohorts with few or no African American women.O

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CONFLICT OF INTEREST STATEMENT

The authors declared no conflicts of interest.

DATA AVAILABILITY STATEMENT

Data are available upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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