Ethnic and Sex Differences in Disease Burden in Patients Undergoing Coronary Angiography: the Confounding Influence of Obesity

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Background: Data from cohort studies, predominantly in Caucasians, have identified obesity as a major risk factor for coronary artery disease (CAD), irrespective of sex. In contrast, reports examining the effects of obesity on mortality in African Americans suggest a weak relationship between body mass index (BMI) and mortality, particularly among women. Data correlating body weight with angiographic severity of CAD is sparse in minority populations. We sought to investigate ethnic-sex differences in the influence of obesity on the extent and severity of CAD.

Methods: We studied 640 patients (66.9% African American) who underwent coronary angiography at a tertiary care center. Cardiovascular risk factor profiles and CAD burden, quantified by the Duke Myocardial Jeopardy scoring system, a validated prognostication tool, were compared across ethnic and sex groups.

Results: Clustering of major cardiovascular risk factors, a higher prevalence of obesity classes II and III, and a statistically significant inverse correlation between BMI and Duke scores were observed among the cohort of African American women. General linear model analysis and stepwise multiple linear regression analysis revealed Duke score to be negatively associated with BMI and higher classes of obesity after adjustment for age and other cardiovascular risk factors in African American women but not in other subgroups.

Conclusions: The observed inverse relationship between BMI and angiographic severity of CAD in African American women is novel and appears to support prior data on the weak association between BMI and cardiovascular mortality in this subgroup. (*Ethn Dis*. 2008;18:53–58)

Key Words: Obesity, Coronary Artery Disease, Race, Ethnicity, Gender, African American, Angiography, Body Mass Index, Myocardial Jeopardy Score

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Introduction

The Framingham study and cohort studies that examined the effects of obesity on cardiovascular morbidity and mortality have consistently reported a positive association between excess body weight and the prevalence of coronary artery disease (CAD) in Caucasian men and women.[1,2] In contrast, several reports of the effects of adiposity on cardiovascular mortality among African Americans suggest that adiposity may be a less important predictor of mortality among African Americans than in Caucasians, particularly among women.[3–10] In fact, the overall relationship between body weight and incident CAD is less well defined for African Americans, and data correlating body weight with the prevalence and angiographic severity of CAD in the African American population are sparse in men[11] and nonexistent in women. We attempted to characterize ethnic-sex differences in the association between body mass index (BMI) and CAD burden as quantified by the Duke Myocardial Jeopardy scoring system, a validated prognostication tool also predictive of one-year mortality in patients treated medically or with percutaneous intervention.[12]

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Methods

We screened 962 consecutive patients who were referred for coronary angiography from January 2005 to October 2005 to a tertiary care referral center. Exclusion criteria included ethnicity other than Caucasian or African American (n=130) and patients with a history of coronary artery bypass graft surgery (n=192). After exclusions, 640 patients made up the final study cohort. Clinical and demographic characteristics including age (in years), ethnicity (Caucasian or African American), sex, diabetes mellitus as per American Diabetic Association (ADA) criteria, dyslipidemia per National Cholesterol Education Program (NCEP) criteria, hypertension per Joint National Committee (JNC 7) criteria, cigarette smoking and family history of CAD were abstracted through a retrospective cross-sectional survey of patient charts. In addition, the use of antihypertensive, antidiabetic, or cholesterol-lowering medications were used as criteria for hypertension, diabetes, and dyslipidemia, respectively. Obesity was classified according to BMI, using the National Institutes of Health (NIH) criteria as normal (BMI 21–24 kg/m^2), overweight (BMI 25–29 kg/m^2), obesity class I (BMI 30–34 kg/m^2), obesity class II (BMI 35–39 kg/m^2), and obesity class III (BMI ≥40 kg/m^2).[23]

Coronary angiography data was obtained from the Siemens Queries software system, which maintains the database that includes detailed angiographic findings of all patients at this institution. Significant lesions were defined as those with >70% diameter narrowing of coronary arteries (>50% for the left main coronary artery). We attempted to quantify severity and extent of CAD by ascertaining the prevalence of high-risk coronary anatomy (defined as >50% stenosis of the left main coronary artery or significant coronary artery disease in three vessels) and by computing myocardial jeopardy scores from anatomic representation of the myocardium at risk, determined by the extent and distribution of coronary lesions. Patients with a history of bypass grafting surgery were excluded from the study because we could not estimate Duke scores in this subset of patients.

In accordance with the Duke Jeopardy Scoring system, the coronary tree was divided into six segments: the left anterior descending coronary artery, diagonal branches, septal perforating branches, the circumflex coronary artery, obtuse marginal branches, and posterior descending coronary artery. Each segment of myocardium distal to 70% stenosis was considered to be at risk and was assigned a score of two. A score from 0–12 was designated to each coronary angiogram based on the number of segments involved.[12] As required by the hospital policy, the institutional review board of the university reviewed and approved our study protocol.

Statistical Analysis

Statistical analyses were performed with the SPSS 13.0 software package (SPSS, Inc., Chicago, Illinois). Continuous (scale) data are presented as mean and standard error (SE). For scale variables, differences in within-group means were assessed by using one-way analysis of variance (ANOVA). For categorical variables, differences in proportion or rate were tested by using likelihood ratio chi-square test. Pearson correlation analysis (r= correlation coefficient) was used to determine unadjusted bivariate correlation between two variables. The aim of the study was to define the association between obesity (BMI) and CAD burden. Because other cardiovascular risk factors like age, diabetes, and hypercholesterolemia contribute to CAD burden, regression analysis was performed with these risk factors as independent variables to define the true association between BMI and CAD burden. Univariate general linear model analysis was performed to identify the independent effect of obesity on coronary lesion severity. Each model was subjected to the Levene test to test the homogeneity of variances. Levene statistic P value ≥.10 was the used to reject the null hypothesis that the groups have equal variances. Finally, after adjusting for age and cardiovascular risk factors), the independent effect of BMI on Duke score was evaluated in multiple stepwise linear regression analysis. A two-tailed P value <.05 was considered statistically significant for all analyses.

RESULTS

The study cohort comprised 640 patients, 53 (8.3%) Caucasian (CA) women, 159 (24.8%) CA men, 197 (30.8%) African American women and 231 (36.1%) African American men. African American women had the highest prevalence of obesity class II and III (Table 1). Clustering of major cardiovascular risk factors was observed among African American women, although the prevalence of smoking was highest among African American men. A trend toward higher prevalence of three-vessel disease was observed in Caucasian men, but the difference did not reach statistical significance. No statistically significant association was observed between ethnic subgroup and prevalence of normal angiogram, one- or two-vessel disease, left main stenosis, high-risk coronary anatomy, or Duke Myocardial Jeopardy score.

On unadjusted bivariate Pearson correlational analysis, a statistically significant weak negative correlation between Duke score and BMI was observed among women but not in men (Figure 1A, B). Stratified by ethnicity, only African Americans showed a weak negative correlation between Duke score and BMI (Figure 1C, D).

In general linear model analysis controlling for other cardiovascular risk factors, obesity class II and III remained independent negative predictors of Duke score in African American women. No independent effect of obesity class on CAD burden was observed in any other sex or ethnic group (Table 2). African American women were more likely to be moderately to severely obese and had the highest mean BMI. When obesity was reclassified according to quartiles of BMI, no independent effect of higher BMI quartiles was observed in Caucasian men, Caucasian women, or African American men; however, in African American women, BMI subclass of higher quartiles remained an independent negative predictor of CAD burden (Table 2)

Because obesity independently correlated with Duke scores in African American women, multiple stepwise linear regression analysis was performed separately for each subgroup. After adjustment for age and other cardiovascular risk factors, BMI remained an independent negative predictor of CAD burden in African American women only (Figure 2). In other strata, no significant association was observed between Duke score and BMI after adjustment for age and other covariates.

DISCUSSION

Our findings emphasize several important points. First, major cardiovascular risk factor clustering and higher prevalence of obesity class II and III were encountered in African Americans, particularly among African American women. Secondly, an inverse weak correlation was observed between BMI

Table 1. Demographic, cardiovascular risk factor, and coronary angiography findings of the study cohort

	Caucasian Women (*n*=53)	Caucasian Men (*n*=159)	African American Women (*n*=197)	African American Men (*n*=231)	*P* value
Age (years)					
Mean (SE)	61.6 (1.7)	60.0 (.9)	61.3 (.9)	59.4 (.8)	.32
Range	34–86	25–83	31–91	30–86	
BMI (kg/m^2)					
Mean (SE)	31.3 (.9)	29.3 (.4)	32.5 (.5)	28.7 (.3)	<.001
Range	(22.6–54.8)	(20.3–42.6)	(18.8–53.5)	(18.9–47.0)	
Percentiles					
25th percentile	25.9	25.7	27.1	24.7	
50th percentile	29.8	28.7	31.2	28.6	
75th percentile	35.0	32.2	36.9	32.1	
Obesity class					<.001
Normal	6 (11.3%)	36 (22.6%)	27 (13.7%)	59 (25.5%)	
Overweight	21 (39.6%)	56 (35.2%)	54 (27.4%)	80 (34.6%)	
BMI class I	13 (24.5%)	48 (30.2%)	53 (26.9%)	61 (26.4%)	
BMI class II	8 (15.1%)	12 (7.5%)	34 (17.3%)	29 (12.6%)	
BMI class III	5 (9.4%)	7 (4.4%)	29 (14.7%)	2 (0.9%)	
Other Major Risk Factors					
Diabetes	16 (30.2%)	36 (22.6%)	99 (50.3%)	82 (35.5%)	<.001
Hypertension	33 (62.3%)	84 (52.8%)	175 (88.8%)	193 (83.5%)	<.001
Smoking	20 (37.7%)	57 (35.8%)	72 (36.5%)	120 (51.9%)	<.001
Dyslipidemia	29 (54.7%)	98 (61.6%)	143 (72.6%)	150 (64.9%)	.04
Family history of CAD	13 (24.5%)	41 (25.8%)	66 (33.5%)	58 (25.1%)	.20
Coronary angiography findings					
Normal angiogram	2 (3.8%)	12 (7.5%)	12 (6.1%)	11 (4.8%)	.62
Left main stenosis	5 (9.4%)	9 (5.7%)	11 (5.6%)	18 (7.8%)	.63
One vessel	27 (50.9%)	71 (44.7%)	96 (48.7%)	108 (46.8%)	.82
Two vessel	16 (30.2%)	39 (24.5%)	52 (26.4%)	64 (27.7%)	.84
Three vessel	3 (6.3%)	28 (18.7%)	26 (14%)	30 (14.1%)	.19
HRCA	8 (15.1%)	37 (23.3%)	37 (18.8%)	48 (20.8%)	.56
Duke Jeopardy Score					
Mean (SE)	4.1 (.4)	3.9 (.2)	3.8 (.2)	4.0 (.2)	.83
Score					.64
0	2 (3.8%)	12 (7.5%)	12 (6.1%)	11 (4.8%)	
2–6	43 (81.1%)	130 (81.8%)	165 (83.8%)	186 (80.5%)	
8–12	8 (15.1%)	17 (10.7%)	20 (10.2%)	34 (14.7%)	

SE= standard error; BMI= body mass index; CAD= coronary artery disease; HRCA= high-risk coronary anatomy.

and CAD burden among African Americans and among women. Third, after adjustment for other cardiovascular risk factors, general linear model analysis revealed that obesity (classes II and III as well as higher obesity quartiles) was an independent negative predictor of Duke score exclusively in African American women. Finally, multiple linear regression analysis revealed that the percentage change in BMI independently (inversely) correlated with Duke score (standardized beta= -0.17, $P<.05$) in African American women. No significant independent association was observed between BMI (or obesity class) and Duke score on multivariate analysis in the rest of the subgroups.

While the literature examining the effects of adiposity on CAD suggest an association between excess body weight, CAD, and all-cause and cardiovascular mortality, these data have largely emerged from cohort studies in Caucasian patients.[1–3] Comparable data from community-based investigations in the African American population suggests a much weaker association between BMI and cardiovascular mortality, particularly among women. Besides, BMI cutoffs associated with equivalent risk across ethnic groups vary considerably depending on the outcome and the risk estimate.[8,14] The failure of BMI and fat patterning to predict mortality in Black women challenge the commonly held assumption regarding the role of obesity in the higher mortality observed in Black women.[3] In another study, CAD risk was associated with central obesity similarly among White and Black men; however, the risk association between central obesity and CAD was weaker for African American women (rate ratio 0.73 vs 1.94 for African American women and Caucasian women respectively).[14] Although BMI has been shown to independently explain

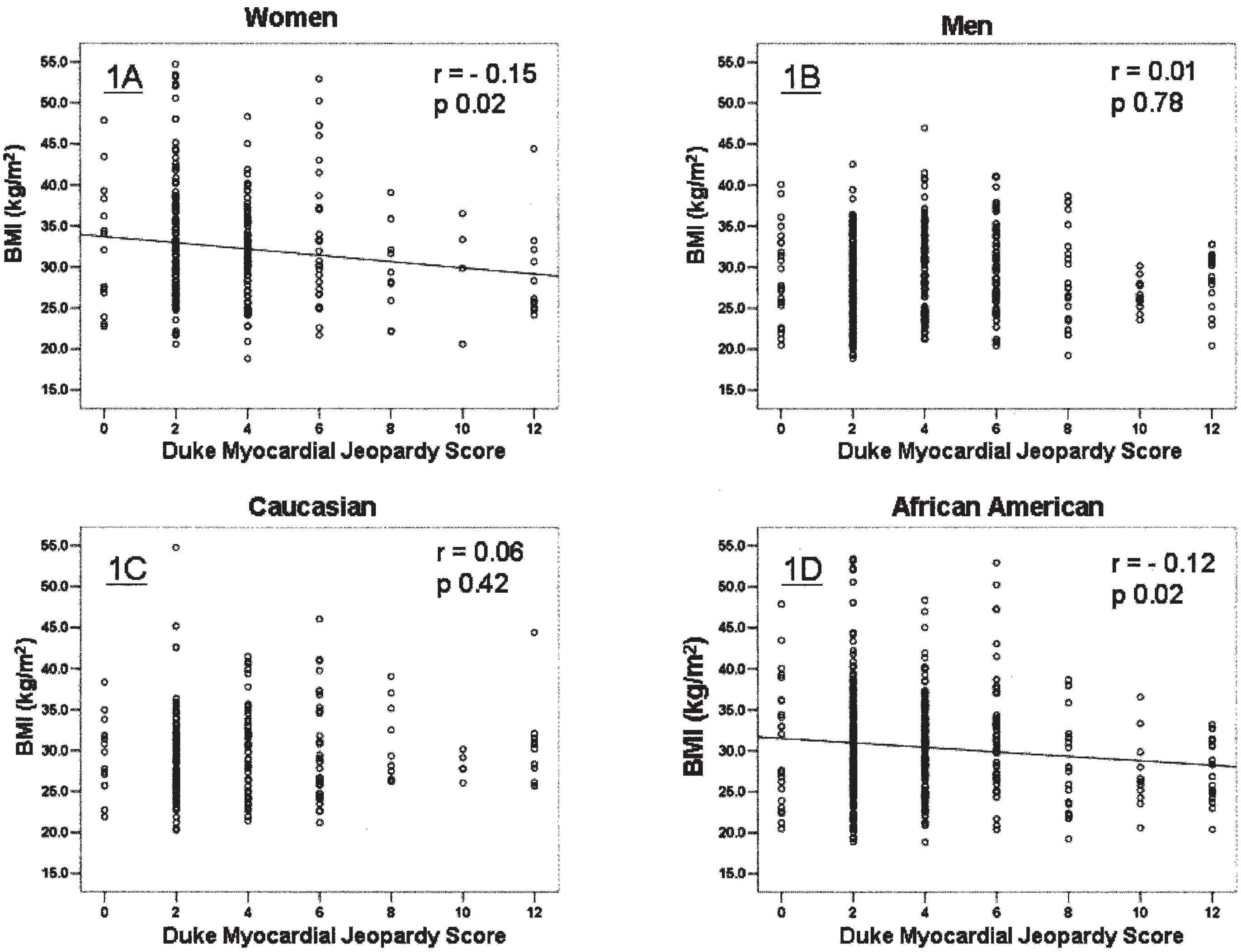

Fig 1. Scatterplots of linear correlation between body mass index (BMI) and Duke myocardial jeopardy score at coronary angiography: BMI correlated negatively with Duke score only in African Americans and women

8% of the variance in incident CAD, primarily in White women,[15] empirical evidence obtained from these studies may not be applicable to a broader population because of the disparity in risk factor intensity between racial groups. We observed the negative correlation between BMI and Duke score to be statistically significant only in African Americans and women. When controlling for age and other major cardiovascular risk factors, obesity class II and III emerged as independent predictors of Duke score in the African American women cohort only. The confounding effect of higher mean BMI among African American women was ruled out when obesity was reclassified according to quartile distribution of BMI. Finally, in linear regression analysis, the negative correlation between BMI and Duke score in African American women remained significant after adjustment for other variables.

Our data suggest that obesity is an independent negative predictor of CAD burden only in African American women. Other determinants of CAD, such as differentially distributed levels of lipoproteins and fibrinolytic activity, may explain the different absolute levels of CAD in this subgroup.[16] Black women tend to have a higher central and abdominal distribution of body fat than do white women.[4,17] Some evidence suggests that the central distribution of fat in Black women may have a weaker effect on atherogenic risk factors such as levels of cholesterol, triglycerides, sex hormone–binding globulin, and the degree of peripheral insulin resistance.[4] More recently, waist-to-hip ratio (WHR)[18] and waist circumference[19] have been touted as superior correlates of cardiovascular risk compared to BMI, and ethnic differences in the extent and distribution of visceral adipose tissue could explain our findings.

Table 2. Independent effect of obesity on CAD burden

	Caucasian Women	Caucasian Men	African American Women	AA Men
Obesity classification				
Normal	Referent	Referent	Referent	Referent
Overweight	1.1 (−2.0–4.1); .47	.6 (−.6–1.7); .34	−.9 (−2.2–.4); .16	0 (−1.0–1.0); .98
Obesity class I	.4 (−2.7–3.6); .79	.5 (−.7–1.8); .41	−.8 (−2.1–.5); .21	.4 (−.7–1.4); .52
Obesity class II	1.5 (−2.2–5.2); .41	1.5 (−.5–3.4); .13	−1.5 (−2.9–.0); <.05*	−.3 (−1.7–1.0); .62
Obesity class III	1.2 (−2.8–5.2); .55	1.5 (−1.0–3.9); .23	−1.6 (−3.1–−.1); <.05*	−1.3 (−5.4–2.9); .55
Levene test for the model	*P*=.86	*P*=.63	*P*=.18	*P*=.57
Obesity Quartile Classification				
1st Quartile	Referent	Referent	Referent	Referent
2nd Quartile	0 (−2.5–2.5); .99	.8 (−.4–2.1); .20	−1.2 (−2.3–−.1); <.05*	0 (−1.1–1.1); .99
3rd Quartile	−.4 (−2.8–2.1); .77	.7 (−.6–1.9); .30	−.9 (−2.0–.2); .11	.3 (−.8–1.4); .54
4th Quartile	.5 (−2.1–3.1); .70	.4 (−.9–1.8); .53	−1.8 (−2.9–−.6); <.05*	−.4 (−1.4–.7); .53
Levene test for the model	*P*=.94	*P*=.31	*P*=.28	*P*=.47

Data are presented as ß coefficient (95% confidence interval); *P* value for the ß coefficient.

Limitations

The study did not address clinical outcomes, including cardiovascular morbidity and mortality. Myocardial infarction frequently develops from angiographically nonobstructive lesions,[20] and we caution against extrapolating angiographic findings to CAD-associated mortality. Nevertheless, our findings support and complement existing literature on the weaker relationship between BMI and mortality in overweight African American women relative to their Caucasian counterparts.[3,6,8,14]

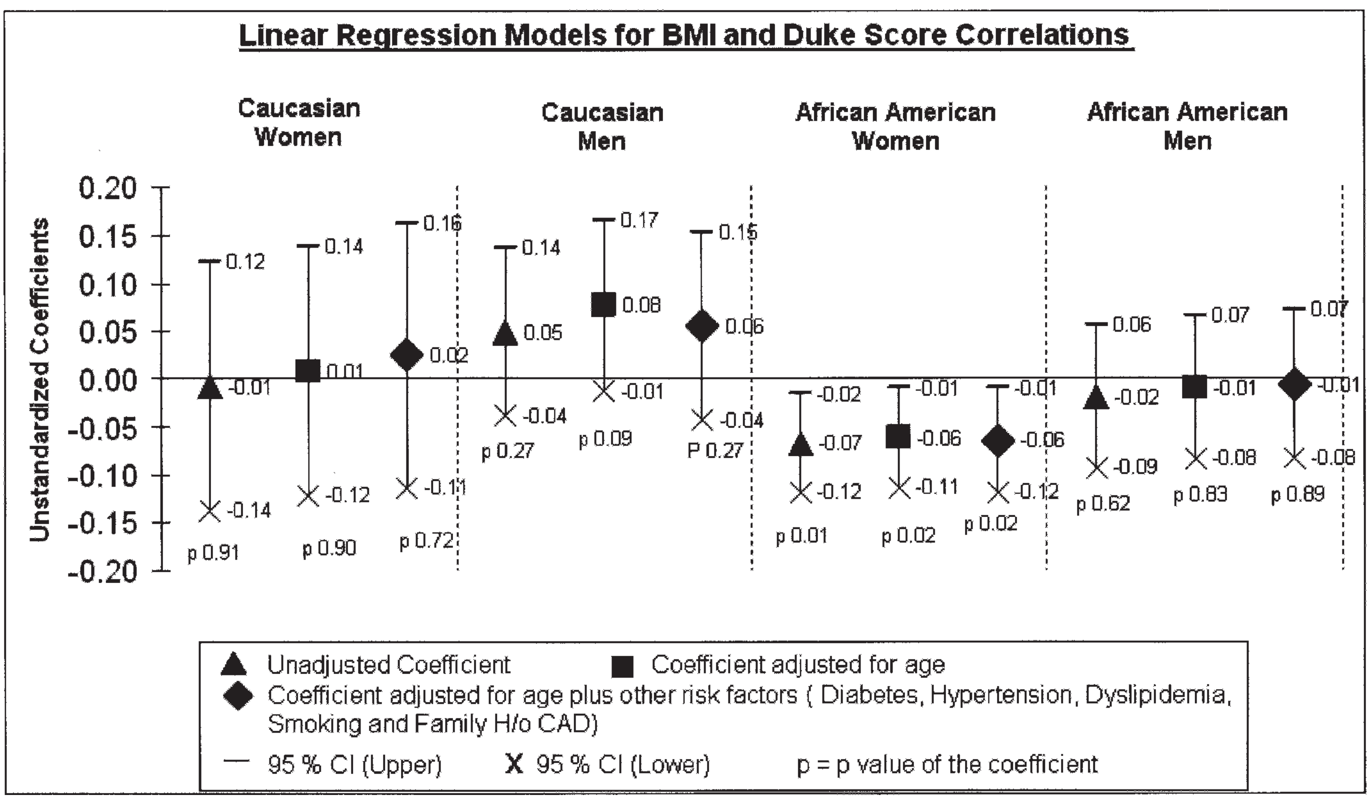

Fig 2. Correlation coefficients from linear regression models relating Duke myocardial jeopardy score to body mass index (BMI) in each subgroup: negative correlation between BMI and Duke score remained significant after adjustment for other cardiovascular risk factors in African women but not in other groups

The relatively small number of Caucasian subjects in our study, primarily reflecting the cross-section of the population served by our institution, is another weakness. Other potentially confounding variables such as other anthropometric indices of obesity (eg, waist-to-hip ratio, waist circumference), physical inactivity, socioeconomic factors, estrogen exposure, hormonal replacement, lipoprotein level, and environmental influences may have affected our results but were not studied, since this data was not readily available. Study participants underwent coronary angiography at a single institution and had a higher pretest probability for CAD; as such, cohort selection bias cannot be excluded. Finally, while our conclusions cannot be extrapolated to the general population, they are hypothesis-generating and deserve future exploration in a larger, multicenter study.

Conclusions

Our findings extend previously reported observations on risk factor clustering in the African American population. The negative correlation between BMI and CAD burden, particularly in African American women, challenge traditional assumptions about the relative risk imparted by obesity and caution against generalizing its influence on cardiovascular risk across sex and racial divides. A better understanding of the risk intensity of established cardiovascular risk factors such as obesity in ethnic minority populations is crucial for finessing risk stratification tools and for the development of population-specific intervention and prevention programs.

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