Relation of Obesity to Circulating B-Type Natriuretic Peptide Concentrations in Blacks

The Jackson Heart Study

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Background—Lower plasma B-type natriuretic peptide (BNP) concentrations in obese individuals (“natriuretic handicap”) may play a role in the pathogenesis of obesity-related hypertension. Whether this phenomenon may contribute to hypertension in blacks is unknown. We tested the hypothesis that body mass index is inversely related to BNP concentrations in blacks.

Methods and Results—We examined the relation of plasma BNP to body mass index in 3742 Jackson Heart Study participants (mean age, 55±13; 62% women) without heart failure using multivariable linear and logistic regression, adjusting for clinical and echocardiographic covariates. The multivariable-adjusted mean BNP was higher for lean participants compared with obese participants in both normotensive (P<0.0001) and hypertensive (P<0.0012) groups. In sex-specific analyses, the adjusted mean BNP was higher in lean hypertensive individuals compared with obese hypertensive individuals for both men (20.5 versus 10.9 pg/mL, respectively; P=0.0009) and women (20.0 versus 13.8 pg/mL; P=0.011). The differences between lean and obese participants were more pronounced in normotensive participants (men, 9.0 versus 4.4 pg/mL; P<0.0001; women, 12.8 versus 8.4 pg/mL; P=0.0005). For both hypertensive and normotensive individuals in the pooled sample, multivariable-adjusted BNP was significantly related to both continuous body mass index (P<0.05 and P<0.0001, respectively) and categorical body mass index (P for trend <0.006 and <0.0001, respectively).

Conclusion—Our cross-sectional study of a large community-based sample of blacks demonstrates that higher body mass index is associated with lower circulating BNP concentrations, thereby extending the concept of a natriuretic handicap in obese individuals observed in non-Hispanic whites to this high-risk population. (Circulation. 2011;124:1021-1027.)

Key Words: diabetes mellitus ■ hypertension ■ natriuretic peptide ■ obesity

Obesity is associated with a state of fluid overload that is characterized by both sodium retention and increased cardiac output.1 The physiological effects of obesity should cause brain natriuretic peptide (BNP) concentrations to be higher with excess adiposity, yet several reports have underscored lower circulating concentrations of BNP in the presence of excess weight. It has been postulated that lower natriuretic peptide concentrations in obese individuals may contribute to the burden of sodium-retaining conditions such as hypertension in these individuals. In a recent study by the Framingham investigators, obese non-Hispanic individuals were found to have circulating natriuretic peptide concentrations that are inappropriately low for the degree of hypertension (Framingham Offspring Study). However, no prior investigation has examined whether the concept of natriuretic handicap in obesity extends to blacks, a group with considerable burden of both obesity and high blood pressure. The availability of routine plasma BNP measurements on >4000 black individuals in the Jackson Heart Study (JHS) allows a comprehensive investigation of the relations of body weight and adiposity to circulating BNP concentrations in this high-risk community and provides

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an opportunity to assess whether hypertension modifies these relations.

**Clinical Perspective on p 1027**

**Methods**

The JHS is a prospective community-based cohort initiated in 2000 to investigate cardiovascular disease in blacks.2 Briefly, ~30% of the JHS participants were former members of the Jackson cohort of the Atherosclerosis Risk in Communities study and had been selected randomly from the drivers’ license registry at the time of the initial recruitment.3 Approximately 23% of those remaining participants were recruited from a commercial listing that represents the overall tricounty population, and another 23% were part of a constrained volunteer sample. The final 24% of the participants were recruited through the JHS Family Study as described previously.4 A total of 3742 JHS participants with plasma BNP measurements were eligible for the present investigation after exclusion of a total of 451 participants owing to missing anthropometric measurements (n=17), renal insufficiency (defined as a serum creatinine >2.0 mg/dL; n=56), morbid obesity (defined as body mass index [BMI] >45 kg/m²; n=215), BNP of 0 pg/mL (n=32) or >100 pg/mL (n=71), and history of heart failure (n=60). Individuals with BNP >100 pg/mL were excluded on the basis of evidence indicating that BNP measurements at this concentration suggest heart failure; this cutoff has a sensitivity of 90%, a specificity of 76%, and a diagnostic accuracy of 81% for diagnosing heart failure in patients presenting to the emergency room with acute dyspnea that is superior to clinical assessment alone.5 All participants underwent a routine physical examination that included a medical history and underwent laboratory assessment for cardiovascular disease risk factors (including plasma BNP concentrations), anthropometry, routine electrocardiography, and echocardiography. We calculated BMI as weight in kilograms divided by height in meters squared. Hypertension was defined as systolic blood pressure ≥140 mm Hg and diastolic blood pressure ≥90 mm Hg, or use of antihypertensive therapy. Diabetes mellitus was defined as fasting plasma glucose ≥126 mg/dL or use of insulin or hypoglycemic medications.

As noted above, participants underwent a standardized 2-dimensional echocardiographic examination. M-mode left ventricular (LV) mass was calculated from the American Society of Echocardiography corrected formula developed by Devereux et al6: Euler (LV) mass was calculated from the American Society of Hypertension corrected formula developed by Devereux et al7:

\[
\text{LV mass} = \frac{1}{0.8} \left[ 1.04 \left( \text{LVDD} + \text{IVS} + \text{PW} \right) - (\text{LVDD})^3 \right] + 0.6, \quad \text{where } \text{LVDD} \text{ is LV diastolic dimension, } \text{IVS} \text{ is interventricular septal wall thickness in diastole, and } \text{PW} \text{ is posterior wall thickness in diastole.}
\]

Left ventricular systolic dysfunction was defined as a fractional shortening <0.29 or a visually estimated ejection fraction <50%. Left atrial dimensions were measured in end systole.

**B-Type Natriuretic Peptide Measurement**

Plasma BNP concentrations were measured in the JHS with a chemiluminescent immunoassay performed on the Siemens Advia Centaur. Quality control samples were assayed within each batch of JHS samples. The coefficient of variation of the assay was measured at 3 concentrations (level 1: mean, 48.47 pg/mL; coefficient of variation, 4.2%; level 2: mean, 472.94 pg/mL; coefficient of variation, 3.1%; level 3: mean, 1810.03 pg/mL; coefficient of variation, 3.4%). The minimal detectable concentration of BNP with this assay was 2.0 pg/mL.

**Statistical Analyses**

We examined the relations of plasma BNP concentrations to BMI using multivariable regression analyses. Plasma BNP concentrations at or below the assay detection limit (2 pg/mL) were considered low (observed in 20% of women and 22% of men) and normal otherwise. Similarly, BMI was treated as a continuous and as an ordinal variable with the World Health Organization/National Institutes of Health classification scheme (normal, <25 kg/m²; overweight, 25.0 to <30.0 kg/m²; obese, ≥30.0 kg/m²). In the obese category, we restricted our analysis to the sample with BMI <45.0 kg/m² (n=3742). Similarly, we used waist circumference (WC) to assess the role of central adiposity, particularly in women. We defined categorical WC as low (WC, <88 cm) and high (WC, ≥88 cm) in women; the corresponding WC cutoffs in men were <102 cm and ≥102 cm.

We performed multivariable linear regression with natural log-transformed BNP as the dependent variable. Tobit models, implemented with the SAS LIFEREG procedure (SAS 9.2), were estimated to account for left censoring of the BNP distribution.8 Regression models included the following covariates: BMI plus age, history of myocardial infarction, diabetes mellitus, current smoking, blood pressure stage (systolic blood pressure <140 mm Hg and diastolic blood pressure <90 mm Hg, systolic blood pressure 140 to 159 mm Hg or diastolic blood pressure 90 to 99 mm Hg, systolic blood pressure ≥160 mm Hg or diastolic blood pressure ≥100 mm Hg, or use of antihypertensive therapy), and serum creatinine in model 1. Additionally, left atrial size, LV mass, and LV systolic dysfunction were included for regression model 2. We also tested for interaction between sex and obesity traits (BMI and WC), but it was excluded in the final analyses because it was not significant. Because we modeled a log-transformed dependent variable, we exponentiated the β-coefficient for BMI to characterize the multiplicative effects of adiposity on BNP concentrations expressed in original units. To accommodate missing data for LV mass, we used an indicator variable (measured LV mass, no/yes) and assigned the mean value in place of missing values. In additional models, we replaced the continuous BMI and WC variables with BMI and WC categories, excluded echocardiographic traits, and repeated the same analyses in the pooled sample. Sex-by-BMI (or WC) interaction was fitted in the case of pooled sample. All analyses were stratified by hypertension status.

**Additional Analyses**

To investigate further the relation between BMI and BNP, we used generalized additive models with a penalized splines smoothing function to fit a curve that describes the relationship between BNP and BMI without assuming a linear relationship.

**Results**

Characteristics of the JHS study sample (mean age, 55±13 years; 62% women) are presented in Table 1. Overall, 1263 participants (34%) were overweight and 1912 participants (51%) were obese. Six percent (n=215) of the participants were determined to be morbidly obese (BMI ≥45 kg/m²) and were subsequently excluded from this analysis. Both the age-adjusted BNP concentration in women and the age- and sex-adjusted BNP concentration for the pooled sample were significantly different across BMI categories (P for trend in both ≤0.001; Table 1).

**Influence of Body Mass Index, Waist Circumference, and Hypertension Status on B-Type Natriuretic Peptide Levels: Multivariable Analyses**

Body mass index was inversely associated with plasma BNP concentrations after adjustments were made in regression models 1 and 2 in the pooled sample with or without stratification by hypertension status (Table 2). In the fully adjusted model, each 1-SD increase in BMI was associated with a statistically significant (P<0.0001) decrease of 13% and 20% in circulating plasma BNP concentrations among hypertensive and normotensive individuals, respectively. This is consistent with a 17% decrement for all participants in the pooled sample. Categorical BMI was also noted to be significantly (P<0.0001) associated with BNP concentration.
Table 1. Demographics of the Jackson Heart Study Participants

<table>
<thead>
<tr>
<th>Age, y</th>
<th>Normal BMI (n=567)</th>
<th>Overweight (n=1263)</th>
<th>Obese (n=1912)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>54±15</td>
<td>56±13</td>
<td>54±12</td>
</tr>
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</table>

- **Men, %**
  - Normal BMI: 47
  - Overweight: 46
  - Obese: 30

- **BMI, kg/m²**
  - Normal BMI: 22.7±1.9
  - Overweight: 27.6±1.4
  - Obese: 35.2±3.8

- **Waist circumference, cm**
  - Normal BMI: 81.8±7.9
  - Overweight: 92.9±8.3
  - Obese: 110.5±14.3

- **Left atrial diameter, cm**
  - Normal BMI: 3.3±0.5
  - Overweight: 3.5±0.4
  - Obese: 3.7±0.4

- **Left ventricular mass, g**
  - Normal BMI: 135.7±30.2
  - Overweight: 147.6±10.4
  - Obese: 153.1±31.4

- **Left ventricular mass index**
  - Normal BMI: 30.7±8.3
  - Overweight: 34.4±8.1
  - Obese: 38.1±9.3

- **Creatinine, mg/dL**
  - Normal BMI: 1.0±0.2
  - Overweight: 1.1±0.2
  - Obese: 1.0±0.2

- **Hypertension, % JHS**
  - Normal BMI: 48
  - Overweight: 58
  - Obese: 67

- **Antihypertensive therapy, %**
  - Normal BMI: 33
  - Overweight: 48
  - Obese: 59

- **Diabetes mellitus, %**
  - Normal BMI: 6
  - Overweight: 15
  - Obese: 23

- **Current smoker, %**
  - Normal BMI: 23
  - Overweight: 13
  - Obese: 11

- **Prior myocardial infarction, %**
  - Normal BMI: 3.9
  - Overweight: 4.7
  - Obese: 4.9

- **Left ventricular systolic dysfunction,* %**
  - Normal BMI: 5.0
  - Overweight: 3.9
  - Obese: 3.5

- **BNP,† pg/mL (n)**
  - Normal BMI: 13.0 (267)
  - Overweight: 10.7 (566)
  - Obese: 9.7 (587)

  Women‡ (n=2322)
  - Normal BMI: 16.0 (300)
  - Overweight: 14.0 (676)
  - Obese: 12.7 (1346)

  All§ (n=3742)
  - Normal BMI: 14.4 (567)
  - Overweight: 12.4 (1263)
  - Obese: 11.2 (1912)

BMI indicates body mass index; JHS, Jackson Heart Study; and BNP, brain natriuretic peptide.

*Measured as fractional shortening <0.29 and ejection fraction <0.50.
†Sex-specific, age-adjusted BNP levels and age- and sex-adjusted BNP levels in women and all participants (P for trend ≤0.0001).
‡P<0.0001.
§P<0.001.

Both hypertensive and normotensive obese participants had lower BNP concentrations compared with hypertensive and normotensive participants with normal BMI (37% and 43% lower concentrations, respectively). Excluding echocardiographic traits from the regression model resulted in a similar significant inverse relation between BNP and BMI; however, the effects were attenuated substantially (Table 2).

Similarly in the pooled sample, WC was inversely associated with plasma BNP concentration in multivariable-adjusted models analyzing continuous and categorical measures. With WC as a continuous measure, each 1-SD increase corresponded to a significant (P=0.0001) 12% and 17% decrement in BNP concentrations among hypertensive and normotensive participants and 15% among the nonstratified sample. In the analysis using categorical measures of WC, normotensive and hypertensive participants with high adiposity had a 26% and 29% lower BNP concentration compared with their counterparts with low adiposity (P=0.0001 and P<0.0001, respectively). The effects of WC were lower in model 2 than in model 1, although the direction of relationship was similar (Table 2).

Figure 1 shows sex-specific multivariable-adjusted mean BNP concentrations by BMI category and hypertension status. Mean BNP levels for lean, overweight, and obese hypertensive participants were 21.9, 18.3, and 14.5 pg/mL for women and 16.6, 11.8, and 9.9 pg/mL for men. Differences in adjusted mean BNP concentration showed that obese participants had significantly (P<0.001) lower adjusted means than lean individuals. Similarly, in normotensive participants, the adjusted mean BNP concentrations for obese men were significantly (P<0.0001) lower than in lean (8.1 pg/mL) than in obese (4.0 pg/mL) participants. The corresponding differences in women were 14.5 pg/mL for lean compared with 9.0 pg/mL for obese (P<0.05; Figure 1).

Figure 2 shows multivariable-adjusted mean BNP concentrations by high and low adiposity for hypertensive and normotensive participants. Hypertensive women with high adiposity had significantly (P=0.002) lower multivariable-adjusted mean BNP levels compared with women with low adiposity category (ie, 16.9 versus 26.3 pg/mL). Corresponding differences in mean adjusted concentrations for men were 11.3 versus 15.9 pg/mL (P=0.0136). These results were replicated in the normotensive group (Figure 2). In normotensive women, the adjusted mean BNP concentration differences between those with low adiposity (14.6 pg/mL) and high adiposity (10.4 pg/mL) were significant (P=0.0153), as was the case in men (6.5 and 4.1 pg/mL; P<0.0001).

The sex-specific relation of BNP to BMI and WC using models with and without echocardiographic traits are shown in Tables I and II in the online-only Data Supplement, respectively.

**Additional Analyses**

In the test for possible nonlinear relationship between BMI and BNP, we observed a highly significant spline smoothing parameter in all participants (P=6.0×10⁻¹⁰), in hypertensive individuals (P=5.0×10⁻⁷), and in normotensive individuals (P=7.2×10⁻³; see Figure 3A through 3C). These results show that the spline for BMI is a strong predictor of plasma BNP concentration. In all cases, BNP decreased with increasing BMI until ≈40 kg/m², at which point it leveled off. This suggests a nonlinear inverse relation between BMI and circulating BNP concentrations.

**Discussion**

**Principal Findings**

Obese and overweight black individuals have considerably lower plasma natriuretic peptide concentrations than individuals with a normal BMI, a finding that is not attributable to underlying differences in cardiovascular risk factors or cardiac structure between obese and nonobese subjects and that extends similar findings in whites. Our findings raise the possibility that augmentation of the natriuretic peptide system may reduce the susceptibility of obese individuals to hypertension. Loss of this protective mechanism may predispose to persistent elevations in blood pressure.

In our study, we found that excluding echocardiographic LV mass and systolic function in the model attenuated the association between BMI (and WC) and BNP concentration. This most likely suggests that echocardiographic traits are true confounders with a strong association with both BMI (seen in previous analysis of this black cohort)⁹⁻¹¹ and BNP (established in previously studies)¹²,¹³

**Previous Studies**

Our findings support that a higher BMI is associated with a lower BNP concentration in community-based participants.
without heart failure, consistent with Framingham findings in non-Hispanic whites. The inverse relation may be due to increased expression of natriuretic peptide clearance receptors by adipose tissue, resulting in increased clearance of BNP in obese subjects. This explanation would also suggest a potential mechanism of hypertension in obese subjects. We note that although the mean adjusted BNP concentrations were similar between hypertensive participants of Framingham and those of the JHS, normotensive individuals in the JHS had lower mean adjusted BNP concentrations compared with Framingham normotensive participants. Although no direct comparison can be made, this finding may be important to blacks at risk of developing hypertension and cardiovascular complications related to hypertension.
Brain natriuretic peptide is adjusted for age, history of myocardial infarction, diabetes mellitus, current smoking, blood pressure stage (systolic blood pressure <140 and diastolic blood pressure <90 mm Hg, systolic blood pressure 140 to 159 mm Hg or diastolic blood pressure 90 to 99 mm Hg, systolic blood pressure ≥160 mm Hg or diastolic blood pressure ≥100 mm Hg, or use of antihypertensive therapy), serum creatinine, echo left atrial size, echo left ventricular mass, and echo left ventricular systolic dysfunction. Multivariable-adjusted means of BNP concentration in lean participants were compared with those of overweight and obese subjects. \( P < 0.05; \) \( ** P < 0.001; \) *** \( P < 0.0001. \)

In the Framingham study, N-terminal proatrial natriuretic peptide concentrations were also lower in individuals with higher BMI, a finding that suggests that decreased release of natriuretic peptide from the heart, rather than increased clearance, may be responsible for the association between higher BMI and lower natriuretic peptide concentrations. Similarly, Dallas Heart Study investigators found a significant association of BMI and natriuretic peptide concentrations. \(^{14}\)

A state of reduced natriuretic peptide concentration also exists in obese individuals with heart failure. In an investigation of 318 patients with heart failure, concentrations of BNP were significantly lower in obese than in nonobese subjects (205±22 and 335±39 pg/mL, respectively; \( P = 0.0007 \)), despite a similar severity of heart failure and cytokine concentrations.\(^{15}\)

**Mechanisms for Reduced Natriuretic Peptide Concentrations in Obesity**

Obesity and elevated BMI have been associated with decreased circulating concentrations of BNP and N-terminal pro-BNP. Obesity has also been well associated with hypertension, salt retention, and increased cardiac output.\(^{3}\) The fact that obesity has been associated with reduced blood concentrations of BNP seems counterintuitive, raising concerns about the diagnostic and prognostic validity of natriuretic peptides in obese patients.\(^{16,17}\)

Several potential theories have been proposed to explain this paradox. One controversial theory is that in obesity there may be increased expression of natriuretic peptide clearance receptors that participate in the removal of natriuretic peptide from the circulation.\(^{18}\) Supporting this hypothesis, elevated natriuretic peptide clearance receptor gene expression has been documented in the adipose tissue of humans with obesity,\(^{19}\) and allelic variants of this gene have been associated with lower plasma natriuretic peptide concentrations.\(^{20}\)

However, reduced concentrations of N-atrial natriuretic peptide in obese individuals whose adipose tissue does not carry clearance receptors suggest that some other nonclearance mechanism probably plays a more prominent role.\(^{8}\) Supporting a nonclearance mechanism is the previously established association seen between higher BMI and lower plasma NT-proBNP, which is structurally distinct from BNP and unlikely to be cleared via natriuretic peptide clearance receptors. One explanation could be that impaired synthesis and secretion of natriuretic peptides from the myocardium rather than clearance receptors contribute more to the relation of increased BMI to low circulating natriuretic peptide concentrations.\(^{8}\) Data supporting suppressed synthesis and/or release of natriuretic peptide from cardiomyocytes have been described in recent medical literature.\(^{14,21}\)

Finally, natriuretic peptide influences lipid and fatty acid metabolism. Framingham investigators recently found that natriuretic peptide levels in their cohort were inversely associated with all components of the metabolic syndrome except for elevated blood pressure and that several metabolic risk factors (including insulin resistance) were associated with low circulating natriuretic peptide levels, even after adjustment for BMI.\(^{22}\) These findings suggest that perhaps BNP may be more a manifestation of metabolic syndrome than related specifically to low BMI.\(^{22,23}\)

**Joint Effects of Obesity and Hypertension on B-Type Natriuretic Peptide Concentrations in the Jackson Heart Study Population**

Although a direct comparison cannot be made, it is true that BNP concentrations were lower in our black cohort compared with that seen in the Framingham Heart Study in all BMI categories among both normotensive and hypertensive individuals.\(^{8}\) One could theorize that the increased risk for hypertension in this ethnic group may be attributed in part to an attenuated compensatory response compared with their white non-Hispanic counterparts.
Brain natriuretic peptide has been found to be effective in lowering blood pressure through its effects on natriuresis, sympathetic tone, and the renin-angiotensin-aldosterone system. Those with hypertension are thought to have higher BNP concentrations as a compensatory mechanism to the high-volume salt retention state of hypertension. Brain natriuretic peptide functions to defend against excess salt and water retention, to inhibit the production and action of vasoconstrictor peptides, to promote vascular relaxation, and to inhibit sympathetic outflow. However, compared with those who are hypertensive and lean, those who are hypertensive and obese appear to have lower BNP concentrations, as observed in our study.

**Study Limitations**

Given our cross-sectional analysis, we cannot infer any causality about the observed inverse relation between body size and BNP. In addition, the JHS is an all-black cohort; therefore, generalizability of our findings to other ethnic groups is limited. However, given these limitations, the strength of our study includes the large community-based sample of blacks.

**Conclusions**

In this community-based cohort of blacks, we established that lower BNP concentrations are associated with increased BMI categories. The relation of lower BNP concentrations with higher BMI categories was present in both nonhypertensive participants and hypertensive participants. Our findings extend the concept of a natriuretic handicap of obesity to blacks.

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Disclosures

None.

References


CLINICAL PERSPECTIVE

In this community-based cohort of blacks, we established that higher body mass index is associated with lower B-type natriuretic peptide concentrations. The relation was present in both sexes and in both nonhypertensive and hypertensive participants. Our findings extend the concept of a natriuretic handicap of obesity to blacks. Augmentation of the natriuretic peptide system may reduce the susceptibility of obese individuals to the development of hypertension; the loss of this protective mechanism may predispose this group to persistent elevations in blood pressure.
Relation of Obesity to Circulating B-Type Natriuretic Peptide Concentrations in Blacks: The Jackson Heart Study


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Supplemental Material
Supplemental Table 1. Sex-Specific Relation of log-BNP to Body Mass Index and Waist Circumference in Hypertensive and Normotensive Jackson Heart Study Participants (Models include Echocardiographic Traits)

Supplemental Table 2. Sex-Specific Relation of log-BNP to Body Mass Index and Waist Circumference in Hypertensive and Normotensive Jackson Heart Study Participants (Models exclude Echocardiographic Traits)
Supplemental Table 1. Sex-Specific Relation of log-BNP to Body Mass Index and Waist Circumference in Hypertensive and Normotensive Jackson Heart Study Participants (Models include Echocardiographic Traits)

<table>
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<th>Models</th>
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WC Categories

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***p<0.0001; ** p<0.001; *p<0.05

Model adjusts for BMI plus age, history of myocardial infarction, diabetes mellitus, current smoking, blood pressure stage (systolic blood pressure <140 and diastolic blood pressure <90 mm Hg; systolic blood pressure 140 to 159 or diastolic blood pressure 90 to 99 mm Hg; systolic blood pressure ≥160 or diastolic blood pressure ≥100 mm Hg, or use of antihypertensive therapy), serum creatinine, echo left atrial size, echo left ventricular mass, and echo left ventricular systolic dysfunction.
### Supplemental Table 2. Sex-Specific Relation of log-BNP to Body Mass Index and Waist Circumference in Hypertensive and Normotensive Jackson Heart Study Participants (Models exclude Echocardiographic Traits)

<table>
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<tr>
<th>Models</th>
<th>Men, β coefficient (SE)</th>
<th>p-value</th>
<th>Women, β coefficient (SE)</th>
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<td><strong>Hypertensive Participants</strong></td>
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<td>Continuous</td>
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<tr>
<td>BMI</td>
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<td>-0.058 (0.028)</td>
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<td>WC</td>
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<td>Reference</td>
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<tr>
<td>Overweight</td>
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<td>BMI</td>
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WC Categories

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***p<0.0001; ** p<0.001; *p<0.05
Model 1 adjusts for BMI plus age, history of myocardial infarction, diabetes mellitus, current smoking, blood pressure stage (systolic blood pressure <140 and diastolic blood pressure <90 mm Hg; systolic blood pressure 140 to 159 or diastolic blood pressure 90 to 99 mm Hg; systolic blood pressure ≥160 or diastolic blood pressure ≥100 mm Hg, or use of antihypertensive therapy), and serum creatinine.