The Relation of Diabetes, Impaired Fasting Blood Glucose, and Insulin Resistance to Left Ventricular Structure and Function in African Americans

The Jackson Heart Study

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OBJECTIVE—We assessed the relation of diabetes and insulin resistance (IR) on left ventricular (LV) structure and function in African Americans.

RESEARCH DESIGN AND METHODS—Among those receiving echocardiograms in cycle 1 of the Jackson Heart Study, we assessed the sex-specific relation of fasting blood glucose (FBG), diabetes, and IR to LV structure and function, adjusting for age, systolic blood pressure, antihypertensive medications, and BMI.

RESULTS—Among 2,399 participants, LV mass index ($P_{women} = 0.0002$ and $P_{men} = 0.02$), posterior wall thickness ($P_{women} = 0.01$ and $P_{men} = 0.05$), and interventricular septal wall thickness ($P_{women} = 0.01$) were related to FBG categories. Among those with normal FBG and no diabetes, concentric remodeling and low ejection fraction in women and LV mass index and posterior wall thickness in men were related to IR.

CONCLUSIONS—In the largest study of its kind in a community-based cohort of African Americans, we found a relation of FBG category and IR to LV structure and function.

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African Americans (AAs) have an increased burden of cardiovascular disease (CVD) and a higher rate of CVD-related deaths relative to non-Hispanic whites, and the course of future CVD death rates remains uncertain partly due to simultaneous increases in diabetes (1). Diabetes may be linked to left ventricular hypertrophy (LVH) and associated adverse cardiovascular outcomes. In the current study, we investigated the relation of fasting blood glucose (FBG) category (normal versus impaired versus diabetes) and insulin resistance (IR) to LV structure and function in AA.

RESEARCH DESIGN AND METHODS

—This study was approved by the Institutional Review Board of Jackson State University, Tougaloo College, and the University of Mississippi Medical Center. Participants gave written informed consent.

Study population
The Jackson Heart Study is a longitudinal community-based cohort study initiated in 2000 focused on understanding CVD distribution and determinants in AA (2). Participants were 18–84 years old and living in the Jackson, Mississippi tricounty area (3).

Clinical covariates
Diabetes was defined as a FBG ≥ 126 mg/dL or a random glucose ≥ 200 mg/dL, history of physician diagnosis of diabetes, or use of insulin or an oral hypoglycemic agent (4). Impaired FBG was defined in those who did not have a diagnosis of diabetes but who did have a FBG of 110 to 125 mg/dL. IR was calculated using the formula for homeostasis model assessment (HOMA-IR) (5).

Echocardiography
Echocardiograms were performed using a Sonos 4500 (Hewlett Packard) ultrasound machine. Final measurements were performed offline by one cardiologist reader who has level 3 training in echocardiography (T.S.). Cardiac dimensions were measured according to the American Society of Echocardiography (ASE) guidelines. Relative wall thickness (RWT) was defined as the ratio of the sum of the posterior wall thickness (PWT) and interventricular septal wall thickness (IVST) to the left ventricular internal diastolic dimension (LVIDD). LVM was calculated from the ASE corrected formula (6).

To correct for body size, LVM index (LVMI) was calculated as LVM (g) divided by height$^{2.7}$ (g/ht$^{2.7}$) (7). For function parameters, fractional shortening (FS) was calculated as: FS = LVIDD − LVISD/LVIDD. LV ejection fraction was measured semi-quantitatively. LV diastolic function parameters were measured using spectral Doppler of mitral inflow velocities and pulmonary vein flow patterns.

Statistical analysis

All analyses were sex-specific. General linear models were used to assess associations with continuous LV structure and function outcome variables, and multiple logistic regression models were used for dichotomous outcome variables. We assessed the relation of these outcomes with predictor variables (FBG category [normal versus impaired versus diabetes] and IR) and clinical covariates (age, systolic blood pressure [BP], mild or greater aortic regurgitation, moderate or greater mitral regurgitation, antihypertensive medication, heart rate, and BMI). Two models were developed for continuous and dichotomous outcome variables, where covariates were adjusted for model 1 excluding BMI, and adjusted for model 2 including BMI. The inclusion of BMI in model 2 was to assess the attenuating effect of BMI.

RESULTS—The analytic study sample comprised 2,399 participants (63% women) who were a mean age of 52 ± 13 years; of these, 74.2% of women and 73.7% of men were in the normal FBG category, 11.8% and 16.1% had impaired FBG, and 14.0% and 10.1% had diabetes, respectively. HOMA-IR scores (median, interquartile [IQR] range) for women and men were 3.36 (IQR, 2.30–5.10) and 2.94 (IQR, 2.11–4.47), respectively.

Across FBG categories, women had higher BMI and lower diastolic BP than men (Table 1).

For women, LVMI, IVST, PWT, RWT, left atrial diameter (LAD), and concentric remodeling (CR) were all significantly greater (in value or prevalence in the case of CR) in higher FBG categories. For men, LVMI, IVST, PWT, LVIDD, LAD, and CR were all significantly greater in the higher FBG categories. Placing BMI in the adjustment attenuated the apparent effect; however, the association remained significant for higher LVMI ($P = 0.0002$), IVST ($P = 0.01$), PWT ($P = 0.01$), for lower prevalence of normal geometry ($P = 0.02$) and higher prevalence of CR ($P = 0.05$) in women, and for higher LVMI ($P = 0.02$), PWT ($P = 0.05$), and LAD ($P = 0.04$) in men. No evidence of an association was found between measures of LV systolic dysfunction or diastolic function with FBG categories in women or men ($P > 0.05$).

In women in the normal FBG category, IR was marginally related to higher RWT ($P = 0.05$) and significantly related to a higher percentage of participants with CR ($P = 0.02$) and lower LV ejection fraction ($P = 0.02$). In women with impaired FBG or diabetes, IVST ($P = 0.02$), PWT ($P = 0.04$), and RWT ($P = 0.04$) were significantly greater with higher quartiles of HOMA-IR score. In men in the normal

FBG category, lower LVMI ($P = 0.03$) and PWT ($P = 0.01$) were related to higher HOMA-IR scores. Men with impaired FBG or diabetes had lower LAD ($P = 0.02$) with higher HOMA-IR scores.

Although systolic BP was associated with metabolic status, the relation between LV structure and metabolic status was not attenuated by controlling for systolic BP.

CONCLUSIONS—Our findings expand current literature on the effects of glucose control and IR on the heart to include a community-based cohort of AA. Investigators in the Framingham Heart Study showed that diabetes and glucose tolerance (GT) were independent contributors to LVM and LV wall thickness in non-Hispanic white women (8). Some studies suggest that GT based on GT testing, which was studied in Framingham, appears to have a slightly greater risk for CVD compared with impaired FBG that was studied in our investigation (9).

Similar to the men in our study, Hypertension Genetic Epidemiology Network (HyperGEN) investigators found a weak relation between IR and LV measures of structure, suggesting a limited role of plasma insulin level on LV remodeling (10). However, different from HyperGEN, we also found a significant,

Table 1—Sex-specific metabolic characteristics in women and men by fasting blood glucose category

Variables	Normal fasting glucose			Impaired fasting glucose			Known diabetes		
	Women (*n* = 1,131)	Men (*n* = 644)	*P*	Women (*n* = 180)	Men (*n* = 141)	*P*	Women (*n* = 214)	Men (*n* = 89)	*P*
Age (years)	50 ± 12	49 ± 13	0.002	59 ± 10	56 ± 12	0.01	58 ± 10	57 ± 12	0.33
BMI (kg/m²)	31.7 ± 7.3	28.5 ± 5.2	<0.0001	34.2 ± 6.2	30.5 ± 5.0	<0.0001	35.5 ± 7.3	32.0 ± 5.4	<0.0001
Waist circumference, in	37.8 ± 6.2	38.1 ± 5.2	0.34	41.2 ± 6.1	41.0 ± 4.7	0.50	42.6 ± 6.1	42.3 ± 5.0	0.64
Systolic blood pressure, mmHg	123 ± 18	124 ± 16	0.14	129 ± 17	130 ± 18	0.66	130 ± 17	133 ± 18	0.13
Diastolic blood pressure, mmHg	78 ± 10	81 ± 10	<0.0001	78 ± 10	82 ± 11	0.0002	77 ± 9	81 ± 10	0.0001
Heart rate, bpm	68 ± 9	65 ± 9	<0.0001	68 ± 9	68 ± 12	0.85	71 ± 10	70 ± 9	0.33
Hypertension, %	48.8	43.3	0.06	76.1	67.4	0.08	87.4	8.0	0.22
Total cholesterol/ high-density lipids	3.7 ± 1.0	4.5 ± 1.4	<0.0001	4.0 ± 1.1	4.7 ± 1.5	<0.0001	3.8 ± 1.1	4.8 ± 1.8	<0.0001
Fasting triglycerides, mg/dL	90 ± 51	106 ± 101	0.0002	111 ± 63	123 ± 82	0.15	126 ± 96	139 ± 130	0.37
Mitral regurgitation, %	2.4	1.6	0.12	1.11	1.42	0.25	1.87	0.00	0.11
Fasting glucose, mg/dL	87 ± 6	88 ± 6	<0.0001	107 ± 6	107 ± 7	0.74	146 ± 60	149 ± 54	0.71
Fasting insulin, IU p50 (25,75p)*	15 (10,18)	13 (9,16)	<0.0001	22 (15,27)	18 (12,22)	0.01	28 (16,32)	38 (13,25)	0.04
HOMA-IR, IU p50 (25,75p)*	2.8 (2.1,4.0)	2.6 (1.9,3.5)	<0.0001	5.2 (3.9,7.2)	4.3 (3.2,5.8)	0.003	7.4 (4.7,12.4)	6.3 (4.3,9.5)	0.27

Data are shown as mean ± SD, unless indicated otherwise. *P* values = comparison by *t* tests, median test (for insulin and HOMAIR-IR) or χ² tests. HOMA-IR, homeostasis model for the assessment insulin resistance. *25,75p = 25th and 75th percentile.

more consistent relation between IR and LV structure and function in women in the normal FBG category and also in those with diabetes, suggesting a potential sex difference in cardiac response to IR.

LVM and geometry may relate to diabetes and IR by their association with elevated systolic BP (11) caused by arterial stiffening. By enhancing LV pulsatile work, increases in end-systolic stress and myocardial oxygen demands through increased pressure may promote cardiac remodeling (12). IR and the accompanying compensatory hyperinsulinemia may result in trophic effects on myocardial tissue; this has been demonstrated in both cell cultures and animal models (13). In addition, LVH may result from sodium retention induced by hyperinsulinemia (12) associated with obesity in participants with impaired FBG and diabetes. Finally, rapid alterations in fatty acid and glucose metabolites within the cardiomyocyte may influence cardiac function (14). Prolonged exposure to hyperglycemia or hyperlipidemia, or both, may lead to lipotoxicity and the development of contractile dysfunction.

Recent statistics on the racial disparity of diabetes mortality in the United States makes clear the need to increase awareness, prevention, and treatment for minorities in particular. Our investigation supports that obesity, diabetes, and IR each influence cardiac structure in AA men and women and cardiac function in a subset of women with IR and normal FBG. Knowing the potential effects on cardiac remodeling and mortality, findings from this study underscore the need for more aggressive management of weight, diabetes, and hyperinsulinemia in this group.

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