Left Ventricular Systolic Dysfunction in a Biracial Sample of Hypertensive Adults

The HyperGEN Study

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Abstract—To determine the prevalence and correlates of left ventricular systolic dysfunction in hypertensive patients in a biracial population-based sample, clinical evaluation and echocardiography were performed in 2086 participants in the Hypertension Genetic Epidemiology Network (HyperGEN) examination; 86% had normal ejection fraction (>54%), 10% had mild ventricular dysfunction (ejection fraction 41% to 54%), and 4% had severe ventricular dysfunction (ejection fraction ≤40%). Prevalences of mild and severe ventricular dysfunction were higher in men than women (14% versus 8% and 7% versus 3%, $P<0.001$) and, weakly, in diabetics than nondiabetics (13% versus 10% and 6% versus 4%, $P=0.07$). Patients with severe ventricular dysfunction were older than those with mild dysfunction or normal function (mean, 58 versus 54 and 54 years, respectively; $P=0.005$) and had higher mean creatinine (1.20 versus 1.05 and 1.00 mg/dL) and uric acid (6.9 versus 6.3 and 6.1 mg/dL) levels (both $P<0.001$). Those with severe ventricular dysfunction, compared with those with mild dysfunction or normal ejection fraction, had greater mean ventricular internal dimension (6.2 versus 5.6 and 5.1 cm) and mass (61 versus 50 and 43 g/m$^{2.7}$) and lower relative wall thickness (0.31 versus 33 and 0.35; all $P<0.0001$). Severe and mild ventricular dysfunction was associated with lower myocardial contractility (mean stress-corrected midwall shortening, 68% versus 94% versus 106% of predicted; $P<0.0001$). In regression analyses, lower ejection fraction as a continuous variable was independently and positively associated with male gender, diabetes, uric acid level, and body mass index. With the addition of echocardiographic variables, lower ejection fraction was associated with male gender, black race, prior myocardial infarction, and higher ventricular mass and lower relative wall thickness, pulse pressure, and body mass index. In a population-based sample of hypertensive patients, left ventricular systolic dysfunction was related to male gender, black race, diabetes, and elevated uric acid levels, as well as higher ventricular mass and lower relative wall thickness. **(*Hypertension*. 2001;38:417-423.)**

Key Words: diabetes ■ diastole ■ echocardiography ■ hypertension ■ ventricular dysfunction

Several reports have established clinical congestive heart failure (CHF) as a potent predictor of cardiovascular mortality.[1–3] Major antecedents of CHF include coronary heart disease, hypertension, and diabetes. Despite progress in controlling hypertension and reducing cardiovascular death rates in the general population, US data show a long-term increase in hospitalizations for CHF.[4,5] Several studies show that CHF increases with advancing age and provide prevalence estimates of 0.2% to 1.5% for symptomatic CHF across the adult age range.[2,3,6,7] However, the proportion of cases of clinical CHF that are due to left ventricular (LV) systolic dysfunction compared with LV diastolic dysfunction, valvular heart disease, or other causes is not well established.[8,9] Furthermore, few data are available on the combined prevalence of symptomatic and asymptomatic LV systolic dysfunction in population samples,[6] especially of high-risk groups such as blacks.[10] With the development of echocardiographic methods that provide a high yield of quantitative LV measurements, it has become possible to determine the prevalence and correlates of LV systolic dysfunction in population-based samples of hypertensive patients.

Accordingly, the present study was undertaken to assess the prevalence and clinical and echocardiographic correlates of mild and severe LV systolic dysfunction in hypertensive black and white women and men participating in the Hypertension Genetic Epidemiology Network (HyperGEN) Study.[11,12] Specific objectives were to (1) determine prevalences of mild and severe LV systolic dysfunction and their

Received November 30, 2000; first decision December 27, 2000; revision accepted February 23, 2001.

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relation to gender, age, race, body build, medication usage, renal function, cardiovascular risk factors, and prevalent disease; (2) determine whether LV systolic dysfunction is associated with diabetes independently of effects of age and obesity; and (3) examine associations of LV systolic dysfunction with measures of LV geometry and valvular function.

Methods

The HyperGEN Study is a component network of the National Health, Lung and Blood Institute Family Blood Pressure Program, which was funded to assess the genetic basis of hypertension in population-based samples. As previously described,[11,12] HyperGEN primarily recruited hypertensive members of sibships in which ≥2 sibs with onset of high blood pressure (BP) without known cause by 60 years of age were willing to enroll in the study. Individuals with type I diabetes were excluded because of the high risk of hypertension resulting from nephropathy. Study participants were recruited, after informed consent was given, from existing populations previously defined and enumerated, including Atherosclerosis Risk in Communities Study sites in Minneapolis, Minn, and Forsyth County, NC; the Minnesota Heart Survey; and the Utah Healthy Family Tree Study. Birmingham, Ga, recruited hypertensives from the community at large. The target population was 100% black in Birmingham, 50% black and 50% white in Winston-Salem (NC), and 100% white in Minnesota and Utah.

The HyperGEN examination obtained standardized measurements of BP at rest and its reactivity to several stimuli. Clinic BP was measured by automated technique, the Dinamap (Critikon, Inc), and was used for all purposes except calculation of LV wall stresses, for which BP measured at the end of the echocardiogram was used. Measurements were made of body mass index, waist-to-hip ratio, and percent body fat by bioelectric impedance; blood samples for fasting glucose, insulin, uric acid, lipid, and lipoprotein concentrations were obtained. Diabetes mellitus was diagnosed by American Diabetes Association criteria (fasting blood sugar level >126 mg/dL or use of hypoglycemic medication).[13] Prevalent myocardial infarction, definite coronary heart disease, and CHF were identified by participant self-reports.

For the present study, 66 of 2152 participants (3%) with echocardiograms without technically satisfactory LV measurements to quantify LV systolic function were excluded. Compared with participants in this study, excluded subjects had higher body weight (104 versus 89 kg) and body mass index (37.2 versus 31.9 kg/m^2), were older (60 versus 54 years, all $P<0.001$), and had higher pulse pressures (64 versus 58 mm Hg, $P<0.01$) but did not differ in gender, race, prevalence of diabetes, height, systolic or diastolic BP, or medications used.

Echocardiographic Methods

Imaging and Doppler echocardiograms were performed by previously described methods.[14,15] A standardized protocol was followed under which the parasternal acoustic window was used to record ≥10 consecutive beats of 2D and M-mode recordings of LV internal diameter and wall thicknesses at or just below the mitral leaflet tips in long- and short-axis views, color flow recordings to search for mitral and aortic regurgitation, and M-mode and 2D short- and long-axis views of the aortic root and left atrium. The apical window recorded ≥10 cycles of 2- and 4-chamber images and color Doppler recordings to assess LV wall motion and identify valvular regurgitation. Studies were recorded on videotape.

Echocardiographic Measurements

Correct orientation of planes for imaging and Doppler recordings was verified as previously described.[16] Measurements were made with a computerized review station. LV internal dimension and septal and posterior wall thicknesses were measured on ≤3 cardiac cycles at end diastole and end systole by American Society of Echocardiography recommendations.[17,18] Use of 2D linear measurements has been previously shown in normotensive and hypertensive adults in our laboratory to yield measurements of LV mass that are interchangeable with those from M-mode measurements ($r=0.967$).

Calculation of Derived Variable

End-diastolic LV dimensions were used to calculate LV mass by a formula that yields values closely related ($r=0.90$) to necropsy LV weight[19]; LV mass measurements derived from M-mode or, when needed, 2D LV linear dimension showed good interstudy reproducibility ($\rho=0.93$) in a separate population of 183 hypertensive patients.[20] Relative wall thickness, LV fractional shortening, and circumferential end-systolic stress (cESS) were calculated by standard methods.[16,21] End-diastolic and end-systolic LV volumes calculated by the method of Teichholz et al[22] were used to calculate LV ejection fraction (EF). Good reproducibility of EF by this method ($\rho=0.68$; 95% confidence interval [CI], 0.60 to 0.75) has been documented,[20] as has accuracy of volume determinations compared with invasive and Doppler reference standards.[23] Partition values were used to separate HyperGEN participants with normal LVEF from those with mild dysfunction (EF ≤54.5%, the lower limit of the 95% CI in 366 apparently normal adults studied in New York[24]) and those with mild dysfunction (40% to 54%) from those with moderate/severe dysfunction (EF <40%). To measure arterial stiffness independently of LV dimensions used to define LV systolic function, stroke volume was also determined by an invasively validated Doppler method.[25] Arterial stiffness was estimated by pulse pressure/stroke volume.[26]

Myocardial contractile efficiency was assessed by examining the relation of midwall fractional shortening (MWS) to midwall cESS measured at the level of the LV minor axis.[21,27,28] MWS was calculated taking into account the epicardial migration of the midwall during systole; cESS was estimated at the midwall by use of a cylindrical model.[27] MWS was expressed as a percent of the value predicted from cESS using a previously reported equation[21] and for convenience was called stress-corrected MWS.

Statistical Analyses

Data are given as mean±SD. Differences between groups classified by levels of LVEF were assessed by ANOVA, followed by the Scheffé post hoc test. Independence of differences from covariates, including antihypertensive and antidiabetic medications, was assessed by the general linear model with Sidak's post hoc test. Independent associations of LVEF with clinical and echocardiographic variables were also assessed by backward multiple linear regression. Because the distribution of LVEF was skewed, regression analyses were repeated using the power of EF (EF$^{2.7}$) that eliminated skewness of the dependent variable, which confirmed the results of primary analyses. Two-tailed $P<0.05$ was considered significant.

Results

Characteristics of Participants

The present report is based on 2086 hypertensive HyperGEN participants 23 to 87 years of age (mean age, 55 years); 1338 (64%) were black and 748 (36%) were white; 1285 were women and 801 were men. A total of 1996 (95.7%) had been treated for hypertension, and 90 (4.3%) were previously untreated; 430 (20.6%) had diabetes (Tables 1 and 2). Doppler echocardiography revealed mild (1+) mitral regurgitation in 330 (15.8%) and ≥2+ mitral regurgitation in 73 (3.5%). A total of 163 participants (7.8%) in the present study reported a history of heart attack, and 45 (2.2%) reported previous CHF. Participants who reported CHF had higher body mass indexes (35.6 versus 32.2 kg/m^2) and wider pulse pressures (65 versus 58 mm Hg, both $P<0.05$) but did not differ in other characteristics.

TABLE 1. Clinical Findings in Hypertensive Women Classified by LV Functional Status

Variable	Normal Function (n=1152)	Mild Dysfunction (n=98)	Severe Dysfunction (n=35)	*P*, ANOVA
Age, y	54±11	53±13	56±10	NS
Body mass index, kg/m^2	32.8±7.5	35.0±9.3	32.3±6.7	0.02
Body fat, %	41±8	42±10	40±8	NS
Systolic BP, mm Hg	132±22	135±25	136±23	NS
Diastolic BP, mm Hg	72±11	72±11	75±14	NS
Pulse pressure, mm Hg	60±17	63±19	61±17	NS
Creatinine, mg/dL	0.93±0.43	0.96±0.62	0.97±0.28	NS
Fasting glucose, mg/dL	112±47	115±50	130±74	NS
Uric acid, mg/dL	5.8±1.6	5.7±1.5	6.4±2.2	0.10
Insulin, mg/dL	10.9±9.8	11.2±10.0	12.1±9.2	NS
Total cholesterol, mg/dL	205±39	201±40	201±47	NS
LDL cholesterol, mg/dL	124±36	122±36	116±44	NS
HDL cholesterol, mg/dL	56±15	55±15	60±17	NS
Triglycerides, mg/dL	132±86	119±63	122±66	NS
CHD, %	7.3	16.7	38.2	<0.001
CHF, %	1.8	3.5	14.7	<0.001
Diabetes, %	21.0	23.5	35.3	NS

CHD indicates coronary heart disease.

Prevalence of LV Dysfunction in Different Subgroups of Participants

LVEF was normal in 1795 (86%), mildly subnormal (EF, 41% to 54%) in 208 (10%), and severely depressed (EF ≤40%) in 83 (4%). Use of more stringent cut points for advanced LV dysfunction revealed that 2.6% had LVEFs <35% and 1.7% had EFs <30%. Men had higher prevalences than women of both mild (13.7% versus 7.6%) and severe (6% versus 2.6%, $P<0.001$) LV dysfunction. Black and white participants had similar prevalences of both mild (10.7% versus 8.6%) and severe (3.9% versus 4.1%) LV systolic dysfunction (P=NS). The gender difference remained significant ($P<0.001$), and the lack of difference between races persisted after exclusion of participants with self-reported myocardial infarction or CHF There were no significant differences among study centers in prevalences of either severe (3.4% to 4.9%) or mild (8.6% to 10.5%) LV dysfunction. Trends toward higher prevalences of severe and mild dysfunction in diabetic participants (5.1% versus 3.7% and 12.1% versus 9.4%) did not attain statistical significance ($P=0.09$). There was no association between LV function status and cigarette smoking. The waist-to-hip ratio increased stepwise from participants with normal LVEFs to those with mild or severe dysfunction (mean, 0.92 versus 94 and 0.95; overall $P<0.001$). Patients with severe LV dysfunction had higher prevalences than those with mild dysfunction or normal LVEFs of mild (1+) mitral regurgitation (27.7% versus 15.9% and 15.3%) and ≥2+ regurgitation (24% versus 3.8% and 2.4%).

Among 2074 subjects supplying such data, prior myocardial infarction was reported by 42% of those with moderate to severe LV dysfunction, 12.5% of those with mild LV dysfunction, and 5.7% of those with normal EF ($P<0.001$). Previous CHF was reported by 15.7%, 4.3%, and 1.3% of participants in the 3 groups defined by LVEF ($P<0.001$). In the groups defined by EF, antihypertensive therapy included β-blockers in 19%, 21%, and 22% (P=NS); calcium blockers in 42%, 42%, and 38% (P=NS); thiazide diuretics in 11%, 22%, and 24% ($P<0.05$); ACE inhibitors in 61%, 36%, and 36% ($P<0.001$); and vasodilators in 3%, 1%, and 1% (P=NS). Antidiabetic treatment included insulin with or without oral hypoglycemic agents in 12%, 11%, and 9% (P=NS) and oral hypoglycemic agents alone in 12%, 11%, and 10% (P=NS).

Clinical Characteristics of Women Classified by LV Function Status

There was no difference among groups in age, whereas body mass index was slightly elevated in women with mild LV dysfunction (Table 1). There was no difference among groups in proportion of treated patients; number of medications used; creatinine, glucose, uric acid, insulin, or serum lipid levels; or proportion of patients taking hypolipidemic medication.

Clinical Characteristics of Men Classified by LV Function Status

Men with severe LV dysfunction were, on average, ≈5 years older than those in the other groups (Table 2). Body mass index was virtually identical in the 3 groups of men, as were systolic, diastolic, and pulse pressures; number of antihypertensive drugs; and fasting glucose or lipid levels. Mean serum creatinine and uric acid levels were higher by ≈20% and 10%, respectively, in men with severe LV dysfunction than those in the other groups.

TABLE 2. Clinical Findings in Hypertensive Men Classified by LV Functional Status

Variable	Normal Function (n=643)	Mild Dysfunction (n=110)	Severe Dysfunction (n=48)	*P*, ANOVA
Age, y	55.1±10.4	55.4±10.9	59.9±9.5*†	0.008
Body mass index, kg/m^2	30.2±5.4	30.7±5.9	29.3±5.6	NS
Body fat, %	28±8	29±9	26±9	NS
Systolic BP, mm Hg	134±20	137±25	133±27	NS
Diastolic BP, mm Hg	79±11	79±14	78±15	NS
Pulse pressure, mm Hg	55±15	58±16	55±19	NS
Creatinine, mg/dL	1.15±0.42	1.14±0.26	1.36±0.82*†	0.005
Fasting glucose, mg/dL	111±43	117±54	111±33	NS
Insulin, mg/dL	10.9±14.4	10.4±9.0	10.3±10.0	NS
Total cholesterol, mg/dL	195±39	194±35	194±38	NS
LDL cholesterol, mg/dL	120±35	120±29	120±36	NS
HDL cholesterol, mg/dL	45±13	45±11	45±15	NS
Triglycerides, mg/dL	154±105	152±110	155±115	NS
Uric acid, mg/dL	6.6±1.6	6.8±1.7	7.3±2.1*	0.013
CHD, %	12.6	23.6*	63.8*†	<0.001
CHF, %	0.5	4.7	17.0*	<0.001
Diabetes, %	17.5	25.0	19.1	NS

*P<0.05 vs normal function group; †P<0.05 vs mild dysfunction group.

LV Characteristics of Women Classified by LV Function Status

There were substantial stepwise increases in LV chamber size and a slight increase in posterior wall thickness from the normal EF group to that with severe LV dysfunction (Table 3). As a result, LV mass and LV mass indexed for body surface area, height$^{2.7}$, and fat-free body mass increased progressively, whereas relative wall thickness fell across the spectrum of LV dysfunction. cESS increased stepwise from the normal EF to severe LV dysfunction group. The increase in afterload, however, did not explain the degree of LV dysfunction, as a result of which stress-corrected LV MWS was ≈15% lower in hypertensive patients with mild LV dysfunction and ≈35% lower in those with EF ≤40% than in the normal EF group. Mean pulse pressure/stroke index was 1.44, 1.55, and 1.62 mm Hg · mL^{-1} · m^{-2} in the 3 groups (P=0.01).

TABLE 3. LV Findings in Hypertensive Women Classified by LV Functional Status

Variable	Normal Function (n=1152)	Mild Dysfunction (n=98)	Severe Dysfunction (n=35)	*P*, ANOVA
EF, %	64±5	50±4	31±7	...
IVS, cm	0.94±0.13	0.96±0.14	0.97±0.12	NS
LVIDd, cm	4.98±0.46	5.50±0.52*	6.13±0.77*†	<0.0001
PWT, cm	0.87±0.11	0.90±0.12	0.91±0.09	0.03
LVIDs, cm	3.23±0.43	4.09±0.44*	5.21±0.79*†	<0.0001
LV mass, g	161±40	196±50*	239±57*†	<0.0001
LV mass/BSA, g/m^2	85±19	100±26*	124±27*†	<0.0001
LV mass/height$^{2.7}$, g/m$^{2.7}$	43.8±11.0	52.3±14.3*	63.2±15.9*†	<0.0001
LV mass/fat-free mass, g/kg	3.27±0.75	3.87±0.98*	4.65±0.97*†	<0.0001
Relative wall thickness	0.35±0.05	0.33±0.05*	0.30±0.05*†	<0.0001
cESS, kdyne/cm^2	154±33	208±40*	298±66*†	<0.0001
MWS, %	18±2	14±2*	9±2*†	<0.0001
Stress-corrected MWS, % predicted	107±11	93±11*	71±14*†	<0.0001
Segmental abnormalities, %	1.1	15.7*	72.7*†	<0.001

IVS indicates interventricular septal thickness; LVIDd, end-diastolic LV internal dimension; PWT, LV posterior wall; LVIDs, end-systolic LV internal dimension; and BSA, body surface area.

*P<0.05 vs normal function; †P<0.05 vs mild dysfunction group.

TABLE 4. LV Findings in Hypertensive Men Classified by LV Functional Status

Variable	Normal Function (n=643)	Mild Dysfunction (n=110)	Severe Dysfunction (n=48)	*P*, ANOVA
EF, %	63±5	49±4	30±7	...
IVS, cm	1.00±0.12	1.00±0.12	1.00±0.15	NS
LVIDd, cm	5.27±0.45	5.76±0.48*†	6.32±0.68*†	<0.0001
PWT, cm	0.93±0.11	0.95±0.10	0.96±0.12	NS
LVIDs, cm	3.46±0.41	4.30±0.42*†	5.41±0.72*†	<0.0001
LV mass, g	191±41	225±49*†	264±52*†	<0.0001
LV mass/BSA, g/m^2	92.0±18.6	107.4±25.0*†	129.9±23.2*†	<0.0001
LV mass/height$^{2.7}$, g/m$^{2.7}$	42.0±9.1	48.8±11.9*†	58.9±11.3*†	<0.0001
LV mass/fat-free mass, g/kg	2.90±0.57	3.38±0.80*†	4.05±0.69*†	<0.0001
Relative wall thickness	0.36±0.05	0.33±0.04*†	0.31±0.05*†	<0.0001
EF	0.63±0.05	0.49±0.04	0.30±0.07	...
cESS, kdyne/cm^2	159±32	217±51*†	285±63*†	<0.0001
MWS, %	17±2	14±1*†	9±2*†	<0.0001
Stress-corrected MWS, % predicted	105±10	94±10*†	65±12*†	<0.0001
Segmental abnormalities, %	1.3	17.2*†	58.7*†	<0.001

Abbreviations as in Table 3.
*P<0.05 vs normal function group; †P<0.05 vs mild dysfunction group.

LV Characteristics of Men Classified by LV Function Status

There were stepwise increases in LV chamber size from men with normal LVEF to those with severe LV dysfunction without significant difference in wall thicknesses (Table 4). As a result, LV mass and LV mass indexes rose across the spectrum of LV dysfunction, whereas relative wall thickness fell. cESS increased stepwise from the men with normal LVEF to those with severe dysfunction. Similar to findings in women, stress-corrected MWS was >10% lower in HyperGEN men with mild LV dysfunction and ≈40% lower in those with severe dysfunction than with normal EF. Pulse pressure/stroke index was 1.40, 1.55, and 1.71 mm Hg · mL^{-1} · m^{-2} in the 3 groups (P<0.001).

Multivariate Analyses

Linear regression models were first developed separately in women and men with LVEF as the dependent variable and independent variables that were significant (P<0.10) in univariate analyses (age, pulse pressure, diabetes, serum creatinine concentration, and uric acid level), as well as body mass index, race, and number of antihypertensive drugs. In women, lower LVEF (in percent) was associated (multiple R=0.20) independently with diabetes (B=−1.28, β=−0.063, P=0.03) and higher body mass index (B=−0.08, β=−0.075, P=0.01). When self-reported myocardial infarction and CHF were also considered, lower LVEF was independently associated (R=0.23) with heart attack (B=−5.7, β=−0.144, P<0.001), CHF (B=−5.3, β=−0.109, P=0.001), and body mass index (B=−0.8, β=−0.073, P=0.038). In men, lower EF was associated (R=0.19) with older age (B=−0.08, β=−0.086, P=0.043), higher uric acid (B=−0.5, β=−0.085, P=0.040), and ACE inhibitor use. When prevalent disease variables were also considered, lower EF was associated (R=0.40) with CHF (B=−16.5, β=−0.277, P<0.001), myocardial infarction (B=−4.8, β=−0.151, P=0.001), and ACE inhibitors (B=−2.3, β=−0.114, P=0.011). When men and women were pooled, clinical variables associated with lower EF (R=0.22) were male gender (B=3.0, β=0.160, P<0.001), higher uric acid (B=−0.03, β=−0.059, P=0.020), diabetes (B=−1.0, β=−0.045, P=0.04), and higher body mass index (B=−0.6, β=−0.048, P=0.04). When prevalent disease variables were also considered, lower LVEF was associated (R=0.32) with prior myocardial infarction (B=−5.7, β=−0.160), male gender (B=−2.7, β=−0.144), CHF (B=−8.7, β=−0.164, all P<0.001), higher body mass index (B=−0.7, β=−0.06, P=0.029), and black race (B=−0.9, β=−0.04, P=0.09). Additional regression analysis considered LV mass and relative wall thickness and clinical findings that were significant in the previous model as independent variables. In this analysis, lower LVEF was associated (multiple R=0.65) with higher LV mass (B=−0.09, β=−0.51), lower relative wall thickness (B=68, β=0.41), self-reported heart attack (B=−2.9, β=−0.083), lower body mass index (B=0.11, β=0.091, all P<0.0001) and pulse pressure (B=0.04, β=0.079, P=0.001), lack of β-blocker use (B=−1.5, β=0.063, P=0.002), black race (B=−1.1, β=−0.049), lack of calcium blocker use (B=−0.08, β=0.043), CHF (B=−2.7, β=−0.050, P=0.02), and male gender (B=−0.9, β=−0.048, P=0.046).

Discussion

The present study represents the first comprehensive assessment of the prevalence and correlates of relatively mild and more severe LV systolic dysfunction in a large population-based sample of hypertensive black and white adults. Multivariate analyses reveal significant associations, independent of previous heart attack or overt CHF, of LV systolic dysfunction with male gender, higher body mass index, and

black race. Taken together with recent evidence of higher mortality in black than white patients with LV dysfunction,[10] this report supports a disproportionate burden from CHF in blacks. In addition, our analyses identified a previously unrecognized, weak association independent of diuretic use between severe LV dysfunction and higher uric acid levels.

Association of Male Gender With LV Systolic Dysfunction

As expected from previous studies,[2–4,6] both mild LV dysfunction and severe LV dysfunction were nearly twice as high in prevalence in male than female HyperGEN participants. In regression analyses controlling for other correlates of LVEF, male hypertensives had mean EFs 2% to 3% lower than hypertensive women. Although the explanation for this gender difference is uncertain, the present analyses show that it is independent of higher prevalences of previous heart attack or episodes of CHF in men. One negative finding, the lack of a relation between BP and reduced LVEF, may be a consequence of near-universal treatment of hypertension in the HyperGEN population and BP reduction by treatment of CHF in some patients with LV dysfunction.

Association of LV Dysfunction With Body Mass Index

An unexpected finding in our primary analyses was the lack of relation between body mass index and LV systolic function. When body mass index was considered in multivariate models, it had variably negative or positive relations with LVEF, depending on whether or not measures of LV geometry were also considered. The explanation for the positive relations observed in the latter situation is uncertain but might be related to an effect of greater venous return related to larger body size acting on LV systolic function via a Frank-Starling mechanism; in addition, individuals with poor cardiovascular health might have suffered parallel reductions in LVEF and body weight.

Relation of LV Function to Metabolic Variables

In view of the important roles of dyslipidemia and abnormal glucose metabolism in the development of coronary atherosclerosis, another notable result of the present study is the lack of relations between LVEF and fasting glucose or lipid levels. This suggests that adverse effects of common dyslipidemias did not play a major role in causing LV systolic dysfunction in HyperGEN participants.

Associations With Diabetes and Age

In univariate analyses, LV systolic dysfunction was weakly associated with older age and diabetes. In multivariate analyses, the association of LVEF with age became nonsignificant, whereas diabetes remained associated with a lower EF by ≈1%. The latter independent relation is consistent with our observations in another population-based study.[29]

Study Limitations

The measure of contractile efficiency we used is— like other indexes that can be applied in diverse, unselected populations—unable to measure LV preload or to manipulate LV load to generate ESS-dimension or ESS-volume relations. The ability of stress-corrected MWS to provide approximate estimates of myocardial contractility, however, is supported by both methodological studies[27,28] and by the relation of this variable to adverse prognosis.[30] In addition, our adjustment for medication use by indicator variables for antihypertensive drug classes could not take into account potentially important effects of drug dose or the time since last medication administration.

Conclusions

LVEF is subnormal, usually without overt CHF, in about 14% of black and white hypertensives in a population-based sample of individuals with mostly treated and reasonably controlled hypertension. Male gender, diabetes, LV hypertrophy, black race, and higher uric acid level were independent correlates of lower EF. Further research is needed to devise and test strategies to prevent the common occurrence of LV systolic dysfunction in patients with hypertension.

Acknowledgments

This work was supported in part by grants RO1-HL-55673 and HL-U10-54471, -54472, -54473, -54495, -54496, and -54509 from the National Heart, Lung and Blood Institute, Bethesda, Md, and grant M10RR0047-34 (GCRC) from the National Institutes of Health, Bethesda, Md. We thank Greg Feitl, Phil Johnson, Amy Haire, and Jan Skuppin for study center coordination; Ruth De Graf, Miguel Espinal, MD, Karen Fowle, Heidi Pollard, Ann Seim, and Wesley Brown for performance of echocardiograms; and Virginia Burns for invaluable assistance in manuscript preparation.

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