Importance of Obesity, Race and Age to the Cardiac Structural and Functional Effects of Hypertension

JOHN S. GOTTDIENER, MD, FACC, DOMENIC J. REDA, MS, BARRY J. MATERSON, MD,
BARRY M. MASSIE, MD, FACC, ALFO NOTARGIACOMO, BS, ROBERT J. HAMBURGER, MD,
DAVID W. WILLIAMS, MS, WILLIAM G. HENDERSON, PhD, for the Department of Veterans
Affairs Cooperative Study Group on Antihypertensive Agents

Washington, D.C.

Objectives. The purpose of this study was to determine the effects of obesity and its interaction with age, race and the magnitude of blood pressure elevation in a large cohort of patients with mild to moderate hypertension and a high prevalence of left ventricular hypertrophy.

Background. Obesity, race and age each have important effects on the incidence and severity of hypertension and may contribute to the effects of blood pressure elevation on the cardiac manifestations of hypertension.

Methods. Left ventricular structure and function were assessed with two-dimensional targeted M-mode echocardiography in 692 men with mild to moderate hypertension (average blood pressure 153/100 mm Hg), and the data were compared in relation to obesity (determined from body mass index), age, race, blood pressure, physical activity, plasma renin activity, urinary sodium excretion, hematocrit, heart rate and serum lipids.

Results. Left ventricular hypertrophy was common (63% with increased left ventricular mass, 22% with left ventricular hypertrophy on the electrocardiogram [ECG]). On multivariable regression

analysis, body mass index was the strongest predictor of left ventricular mass and magnified the slope relation of blood pressure to left ventricular mass. Despite a greater prevalence of ECG left ventricular hypertrophy in blacks (31%) than in whites (10%), left ventricular mass and echocardiographic prevalence of left ventricular hypertrophy did not differ by race. However, septal, posterior left ventricular and relative wall thickness were greater in black than in white men.

Conclusions. Obesity is the strongest clinical predictor of left ventricular mass and left ventricular hypertrophy in men, even in those with mild to moderate hypertension of sufficient severity to be associated with a high prevalence of left ventricular hypertrophy. Moreover, independent effects of systolic blood pressure on left ventricular mass are amplified by obesity. Although race does not affect left ventricular mass or the prevalence of left ventricular hypertrophy, black race is associated with greater relative wall thickness, itself a predictor of unfavorable cardiovascular outcome.

(J Am Coll Cardiol 1994;24:1492–8)

In patients with hypertension, the presence of left ventricular hypertrophy is an important independent predictor of morbidity and mortality (1–4). Moreover, increased left ventricular wall thickness relative to cavity size ("concentric" left ventricular hypertrophy) confers additional risk even in the absence of hypertrophy (3).

Although elevated blood pressure is considered to be an important factor promoting left ventricular hypertrophy, only a portion of the observed variance in left ventricular mass is accounted for by blood pressure. Other clinical descriptors that

have been implicated (5–16) as contributors to left ventricular hypertrophy include obesity, age, race, dietary sodium intake, insulin resistance and other neurohormonal factors including adrenergic factors and the renin-angiotensin system. However, the findings of previous studies, some limited to relatively few subjects or small numbers of black patients, have often been inconsistent. Moreover, many prior studies of the effects of biologic and population descriptors on left ventricular structure and function have been conducted in separate groups of patients, usually with relatively mild hypertension, a low prevalence of left ventricular hypertrophy or only a small number of African-American subjects.

The present study group comprises a large number of men, wide age range, approximately equal racial proportion, as well as high average level of blood pressure and high prevalence of left ventricular hypertrophy on electrocardiogram (ECG) and echocardiogram. The group provided a unique opportunity to test the hypothesis that in male patients with mild to moderate hypertension, obesity, race, age and other descriptors affect left ventricular mass and function independently of blood pressure

Figure 1. Left ventricular architecture characterized by relation of wall thickness to cavity size. LVDD = left ventricular diastolic cavity dimension in diastole alone and after indexing (LVDDI) for body surface area; LVH = left ventricular hypertrophy.
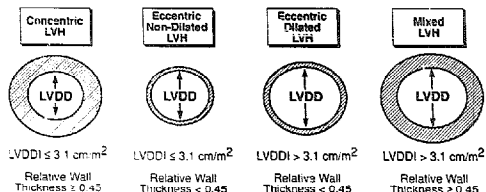
and modify the relation of blood pressure itself to left ventricular mass.

Methods

Patients. The study group was part of a larger cohort of 1,292 men recruited for a placebo-controlled, multicenter, seven-limb, double-blind randomized prospective trial (17) of monotherapy in mild to moderate hypertension (diastolic blood pressure 95 to 109 mm Hg; average blood pressure 153 ± 14/100 ± 4 mm Hg) uncomplicated by clinically evident cardiac or systemic disease. Of 1,292 men included in the primary study, echocardiograms in 692 (54%), acquired at 14 centers, were utilized for this study. This number reflects the product of the overall acquisition rate (72%) and the proportion of technically acceptable studies (75%) for the estimation of left ventricular mass.

Echocardiography. After 6 to 12 weeks of withdrawal of prior antihypertensive therapy (460 patients) or 4 to 12 weeks of baseline observation in the 232 patients not receiving therapy at study entry, two-dimensional targeted M-mode echocardiography was performed. Measurement of ventricular septum, left ventricular cavity and posterior wall dimensions from paper strip chart recordings were performed by a single reader, utilizing an offline image analysis system, according to American Society of Echocardiography (ASE) criteria (18). Left ventricular mass (ASE criteria) was calculated as described elsewhere (19). For comparison with subjects in a normal population, ASE left ventricular mass measurements were also converted to Cornell-Penn convention values utilizing published regression equations (20). For determination of the presence of left ventricular hypertrophy, left ventricular mass (Cornell-Penn criteria) was indexed to body surface area, computed by nomogram (21); 134 g/m² was selected as the partition value for left ventricular hypertrophy (19). Additionally, to avoid the flattening contribution of obesity to the estimation of left ventricular hypertrophy prevalence, left ventricular mass (ASE criteria) was also indexed to height according to the Framingham convention (22); 164 g/m was selected as the partition value for left ventricular hypertrophy. Relative left ventricular wall thickness was expressed as the ratio of twice the left ventricular posterior wall thickness to left

ventricular diastolic cavity dimension; <0.45 was selected as the partition value for normal (20).

Left ventricular architecture (23) in patients with hypertrophy (Framingham criteria) was characterized by the relations of septal wall thickness, posterior wall thickness and left ventricular cavity dimension in diastole (Fig. 1). "Concentric remodeling" (24) of the left ventricle was defined as increased relative wall thickness in the absence of increased left ventricular mass/height.

Meridional left ventricular end-systolic wall stress, left ventricular fractional shortening, cardiac output and peripheral resistance were computed as described previously (25). The relation of fractional shortening to end-systolic stress has been shown (25,26) to be a relatively load-independent index of left ventricular contractile state. Hence, the effects of obesity, race and age on the end-systolic stress–left ventricular fractional shortening relation were determined.

Adiposity. Body mass (Quetelet) index was selected as a measure of adiposity (27,28), determined as weight (kg) divided by height (m) squared. *Normal weight* was defined by body mass index <27 kg/m² (269 patients), *overweight* as 27 to 30 kg/m² (200 patients) and *obesity* as >30 kg/m² (223 patients).

Clinical measurements. Casual blood pressure was measured with cuff sphygmomanometer after 15 min of rest, sitting upright with the back supported. The value used reflected the average of six readings with three readings taken at each of the last two baseline visits. Plasma renin was determined by iodine-125 radioimmunoassay (Clinical Assays, Travenol Division, Genentech Diagnostics, Inc). Physical activity index was obtained by an administered questionnaire that queried subjects on work and recreational physical activity during the 6 months before recruitment to the study. Sodium intake was determined from one 24-h measurement of total urinary sodium excretion (mmol). Comparison of total urinary sodium excretion with left ventricular mass was made only in those 420 patients with complete 24-h urine collections.

Statistical methods. All values for quantitative measures are expressed as the mean value ± SD. Data for outcome variables (e.g., left ventricular mass) were compared (29) across more than two groups (e.g., normal weight, overweight, obese) by utilizing analysis of variance (ANOVA) for unbalanced data. Pairwise comparison of groups was made by using

the Tukey procedure if the ANOVA statistic was significant at the 0.05 level.

Comparisons across two groups (e.g., black men, white men) were performed by using the Student t test (two-tailed) for independent groups.

Distribution of noncontinuous variables was compared across groups by using the chi-square test of homogeneity for contingency tables. If significant differences were present, the Grizzle-Starmer-Koch approach (30) was used to identify which pairs of groups were different.

Univariate relation of clinical variables to left ventricular mass was examined by using least squares linear regression, and the independent contribution of clinical descriptors, including adiposity, race, age and physical activity, to left ventricular mass was determined by stepwise multiple regression.

To determine the effects of obesity, race and age on left ventricular systolic function, analysis of covariance (ANCOVA) was employed to determine whether the slope between fractional shortening and end-systolic wall stress was modified by body mass index, race or age. Body mass index and age were tested both as categoric variables with ANCOVA and as continuous variables by using a linear regression approach to examine the relation established with ANCOVA.

The statistical computer package SAS, versions 5 and 6 (29), was used to generate the statistical analyses. All statistical tests were two-tailed; $p \leq 0.05$ was used to identify statistically significant results.

Results

Left ventricular mass and left ventricular hypertrophy. For all patients the average left ventricular mass indexed for body surface area (Cornell criteria) was 136 ± 39 g/m^2 and indexed for height (Framingham criteria) was 187 ± 51 g/m. Compared with patients with technically adequate echocardiograms, those with uninterpretable studies were older (64 ± 9 vs. 58 ± 11 years, p = 0.0001), slightly heavier (91.4 ± 17.7 vs. 89.1 ± 15.5 kg, p = 0.045) and more frequently white (42% vs. 20%, $p < 0.0001$). The prevalence of left ventricular hypertrophy was highly dependent on the criteria used: 63% utilizing Framingham criteria and 46% utilizing Cornell criteria.

The strongest bivariate relations of left ventricular mass were with body mass index (r = 0.355, p < 0.0001) and body weight (r = 0.329, p < 0.0001); the relation with systolic blood pressure was weaker (r = 0.186, p < 0.0001). Diastolic blood pressure was not significantly related to left ventricular mass/height, possibly because of range restriction resulting from the diastolic blood pressure entry criteria. Physical activity score, plasma renin, hematocrit and sitting pulse rate showed a weak but significant inverse univariate association with left ventricular mass/height.

Of patients with left ventricular hypertrophy (Framingham criteria), 58% had concentric, 8% had eccentric-dilated, 34% had eccentric-nondilated and 1% had mixed left ventricular hypertrophy. Disproportionate increase in septal thickness was present in 10% of patients with left ventricular hypertrophy,

most of whom (72%) had concentric left ventricular hypertrophy. Moreover, of 256 patients without left ventricular hypertrophy, 115 (48%) had evidence of "concentric remodeling" (24) (average relative wall thickness 0.56 ± 0.11). Hence, only 141 (20%) of 692 patients with m ld to moderate hypertension were free of any evidence of left ventricular structural alteration.

Obesity and left ventricular mass. There were marked differences (Table 1) in left ventricular mass/height according to adiposity category (p < 0.001, ANOVA) but smaller intergroup differences between obesity categories when left ventricular mass was indexed for body surface area rather than height (p = 0.032 ANOVA). The prevalence of left ventricular hypertrophy increased markedly in overweight and obese patients (p < 0.05 for all pairwise comparisons), in contrast to modest increases utilizing Cornell criteria (Fig. 2).

In patients with left ventricular hypertrophy, obesity had significant effects on left ventricular architecture (Fig. 3). Although concentric left ventricular hypertrophy was most prevalent in all body mass index groups, the proportion of eccentric-nondilated left ventricular hypertrophy increased with body mass index.

Race and left ventricular mass. Left ventricular mass and left ventricular mass indexed by either height or body surface area did not differ by race, although septal thickness, posterior wall thickness and relative wall thickness were all significantly greater in black men (Table 1). Although the presence of left ventricular hypertrophy on ECG in blacks (31%) was threefold greater than in whites (10%, p < 0.001), there was no difference in the prevalence of left ventricular hypertrophy on echocardiogram (65% in blacks vs. 61% in whites, p = 0.227). Additionally, there were no significant racial differences in the prevalence of disproportionate septal thickening (blacks 7.4%, whites 5.5%, p = 0.738).

Age and left ventricular mass. Left ventricular mass index increased with age (Table 1) as did relative wall, septal and posterior wall thickness, whereas diastolic left ventricular cavity size was unchanged. There were no significant differences in left ventricular hypertrophy architecture between age groups.

Left ventricular mass: interaction of blood pressure, race, age and obesity. On stepwise multiple regression (Table 2), body mass index and systolic blood pressure were independently associated with left ventricular mass/height. Hematocrit and physical activity retained weak negative associations. There was a strong interaction of the effect of systolic blood pressure with the effect of body mass index on left ventricular mass/height such that much stronger effects of systolic blood pressure on left ventricular mass occurred in patients who were obese or overweight than in those who were of normal weight (Fig. 4). This effect of obesity in increasing the slope of the relation between systolic blood pressure and left ventricular mass was also present for septal and posterior left ventricular wall thickness.

Whereas age and race were not independent predictors of left ventricular mass/height, race (black), age, pulse rate at

Table 1. Cardiac Structural and Functional Characteristics in 692 Men With Mild to Moderate Hypertension

	Body Mass Index (kg/m²)				Age (yr)					Race		
	<27	27–29	≥30	p Value*	<50	50–59	60–69	≥70	p Value*	Black	White	p Value†
LV diastolic dimension (mm)	49.6 ± 5.9	51.3 ± 6.2	52.5 ± 6.3	<0.001	52.2 ± 5.9	50.5 ± 6.0	50.9 ± 6.5	50.3 ± 6.0	0.067	50.9 ± 6.0	51.3 ± 6.5	0.224
LV septal wall (mm)	12.7 ± 2.3	13.1 ± 2.2	13.4 ± 2.3	0.004	12.5 ± 2.2	12.9 ± 2.1	13.2 ± 2.4	13.7 ± 2.4	<0.001	13.2 ± 2.3	12.9 ± 2.3	0.046
LV posterior wall (mm)	11.8 ± 2.0	12.4 ± 2.1	12.5 ± 2.2	<0.001	11.5 ± 1.9	12.1 ± 1.9	12.5 ± 2.3	12.5 ± 2.0	<0.001	12.4 ± 2.2	12.0 ± 2.0	0.024
Relative wall thickness	0.48 ± 0.11	0.49 ± 0.11	0.48 ± 0.11	0.970	0.45 ± 0.09	0.48 ± 0.10	0.50 ± 0.13	0.51 ± 0.11	<0.001	0.49 ± 0.12	0.47 ± 0.10	0.034
LVM/height (g/m)	170 ± 44	190 ± 46	204 ± 58	<0.001	160 ± 41	180 ± 42	181 ± 56	193 ± 55	0.010	189 ± 50	185 ± 54	0.367
LVM (Cornell) (g/m²)	132 ± 37	140 ± 39	139 ± 40	0.032	129 ± 35	133 ± 34	141 ± 42	141 ± 39	0.010	137 ± 38	134 ± 40	0.112
Systolic BP (mm Hg)	153.0 ± 14	153 ± 14	151 ± 13	0.238	144 ± 11	151 ± 13	156 ± 13	160 ± 13	<0.001	153 ± 14	153 ± 13	0.062
Diastolic BP (mm Hg)	100 ± 4	100 ± 3	99 ± 3	0.360	100 ± 4	100 ± 4	99 ± 3	100 ± 4	0.003	100 ± 4	99 ± 3	0.306
HR, sitting (beats/min)	74 ± 10	74 ± 11	74 ± 11	0.789	76 ± 11	75 ± 11	73 ± 11	73 ± 11	0.028	75 ± 11	73 ± 11	0.237
Cardiac output (liters/min)	7.54 ± 2.26	8.31 ± 2.51	8.63 ± 2.84	<0.001	8.84 ± 2.64	8.04 ± 2.46	8.09 ± 2.60	7.96 ± 2.36	0.166	8.24 ± 2.74	8.20 ± 2.74	0.858
Peripheral resistance (dynes·cm⁻⁵)	1,430 ± 633	1,240 ± 401	1,173 ± 440	<0.001	1,159 ± 348	1,209 ± 460	1,329 ± 535	1,453 ± 448	0.003	1,298 ± 535	1,277 ± 482	0.899
Fractional shortening (%)	37 ± 8	39 ± 7	38 ± 7	0.146	37 ± 6	38 ± 7	39 ± 8	38 ± 4	0.039	37 ± 7	39 ± 7	0.044
Weight (kg)	76.4 ± 8.6	89.1 ± 7.3	104.1 ± 14.1	—	93.4 ± 19.1	88.6 ± 14.1	87.3 ± 15.0	85.9 ± 12.3	<0.001	89.5 ± 16.8	88.0 ± 14.1	0.378
Body mass index (kg/m²)	24.6 ± 1.9	28.5 ± 0.9	33.8 ± 3.8	—	29.6 ± 3.3	28.6 ± 4.4	28.6 ± 4.5	26.0 ± 3.6	0.067	28.8 ± 5.0	28.5 ± 5.0	0.433
Age (yr)	58.3 ± 9.9	59.2 ± 10.0	55.9 ± 11.0	0.003	41.1 ± 5.5	55.4 ± 2.6	64.2 ± 2.7	72.4 ± 2.3	—	57.3 ± 10.8	58.7 ± 9.5	0.166

*ANOVA. †Impaired t test. BP = blood pressure; HR = heart rate; LV = left ventricular; LVM = left ventricular mass; LVMI = left ventricular mass index.
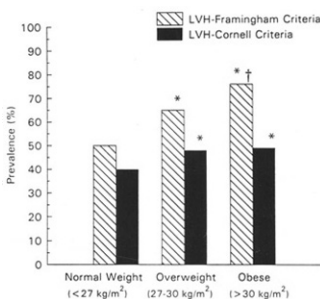

Figure 2. Prevalence of left ventricular hypertrophy (LVH) according to body weight category. *p < 0.05 versus normal weight. †p < 0.05 versus overweight.

rest, and plasma renin activity were independent predictors of relative wall thickness.

Left ventricular function. Left ventricular fractional shortening was within normal limits (≥28%) in 559 (92%) of 609 men in whom it could be measured and did not differ across adiposity groups. A substantial decrease in fractional shortening (≤21%) was noted in only 6 patients (1%).

There was a good correlation between fractional shortening and end-systolic stress (r = −0.733, p = 0.0001), with a slope estimate for end-systolic stress of −0.28. On ANCOVA, there was no relation between fractional shortening and race, body mass index or age. Moreover, none of these affected the slope estimate of fractional shortening for end-systolic stress. Hence, the relation between fractional shortening and end-systolic stress was the same across race, age and body mass index.

Discussion

A principal result of this study was that, even in men with established hypertension and a high prevalence of left ventric-

Figure 3. Left ventricular architecture according to body weight category. Ecc = eccentric.
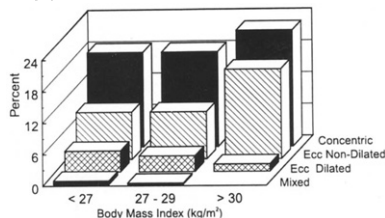
Table 2. Stepwise Multiple Regression for Left Ventricular
Mass Variables

	Left Ventricular Mass/Height			
	Variable Estimate	Partial R^2 Value	F Value	p Value
Intercept	49.45			
Body mass index	4.22	0.122	84.4	0.0001
Systolic BP	0.54	0.035	24.7	0.0001
Hematocrit	−1.70	0.019	13.9	0.0002
Physical activity	−0.06	0.008	6.1	0.01
Age	0.33	0.005	3.6	0.06
HDL	0.30	0.004	3.1	0.08
Plasma renin activity	−1.25	0.003	2.2	0.14
Pulse rate	−0.24	0.002	1.7	0.19

BP = blood pressure; HDL = high density lipoprotein.

ular hypertrophy, obesity was the strongest independent predictor of left ventricular mass and the presence of left ventricular hypertrophy. Moreover, obesity increased the slope of the regression between systolic blood pressure and left ventricular mass, thus magnifying the relation between blood pressure and left ventricular mass. Relative to the marked effect of obesity, systolic blood pressure, increasing age, sodium excretion and race were weaker determinants of left ventricular mass and prevalence of left ventricular hypertrophy.

The present study results differ in several important ways from previous studies that have shown association of obesity with left ventricular mass: the components of left ventricular mass that are involved, the relation of left ventricular mass to systolic versus diastolic pressure and the roles of race and age.

Previous studies of obesity and left ventricular mass. In a previous study of normal subjects and patients with hypertension (8), obesity was associated with eccentric left ventricular hypertrophy consequent to left ventricular cavity dilation; diastolic rather than systolic blood pressure was predictive of left ventricular hypertrophy, and left ventricular mass was not greater in lean hypertensive patients than in lean normotensive subjects. Hammond et al. (31) also found that increased left

Figure 4. Effect of obesity on relation between systolic blood pressure and left ventricular (LV) mass. Body weight categories as in Figure 2.

ventricular mass with obesity was a consequence of left ventricular cavity dilation, but not increased wall thickness. In the Framingham Heart Study (5,9), which utilized echocardiography in a large population-based cohort, obesity measured by body mass index or by skinfold thickness was associated with substantial increases in the prevalence of left ventricular hypertrophy in men. Systolic, but not diastolic, blood pressure was also independently predictive of left ventricular hypertrophy. Whereas both hypertension and obesity were independently associated with left ventricular mass and wall thickness, the associations were additive but not synergistic. Recently, Liebson et al. (10) noted that in patients with mild hypertension and virtual absence of left ventricular hypertrophy on ECG, that body weight and body mass index were important predictors of left ventricular wall thickness, mass and hypertrophy on echocardiogram. However, eccentric dilated hypertrophy was the most common pattern (52%) of left ventricular hypertrophy, followed by concentric left ventricular hypertrophy (33%).

In contrast, we found in the present study that both left ventricular wall thickness and left ventricular cavity volume were greater in obese and overweight hypertensive men than in men of normal weight. Moreover, despite the importance of obesity in the cohort, even lean hypertensive men with mild to moderate hypertension had a high prevalence of left ventricular hypertrophy. Also, relative wall thickness was equally increased in all adiposity groups. Hence, we found mostly concentric hypertrophy even in obese men with mild to moderate hypertension. In this patient cohort, differing substantially from that of Framingham, our findings support a synergistic effect of obesity and hypertension on left ventricular mass and hypertrophy.

Race and left ventricular hypertrophy. The prevalence and severity of hypertension are greater in blacks than in whites (32,33), and ECG studies (4,34) have suggested a greater prevalence of left ventricular hypertrophy as well. However, utilizing echocardiographic left ventricular hypertrophy as a reference standard, Lee et al. (34) found that the specificity of ECG criteria for left ventricular hypertrophy, not adjusted for race, is lower for blacks than for whites. Hence, although the ECG prevalence of left ventricular hypertrophy was two- to sixfold greater in blacks, on the basis of the criteria used, the prevalence of left ventricular hypertrophy on echocardiogram did not differ. In the present study, we also found a marked racial disproportion in the ECG prevalence of left ventricular hypertrophy, despite the absence on echocardiogram of racial differences in either left ventricular mass or prevalence of left ventricular hypertrophy.

One study (35) of a relatively small number of black and white hypertensive subjects found greater left ventricular mass in blacks consequent to greater left ventricular cavity size. However, the study did not control for possible racial differences in obesity. Several other studies (10,11,36) have not shown higher left ventricular mass in blacks, although greater septal wall thickness and relative wall thickness in blacks have been noted (11).
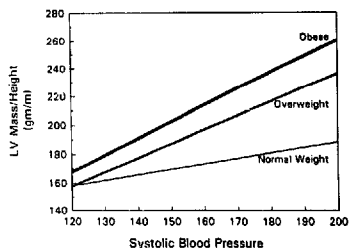
In evaluating patients differing substantially in number or in characteristics from those of previous studies, we found no racial difference in left ventricular mass or prevalence of left ventricular hypertrophy on echocardiogram. However, black men did have greater septal wall, posterior wall and relative wall thickness than did white men.

Age and left ventricular hypertrophy. Previous studies (5,10,12,14,37) have differed in their findings on the independence of the relation between age and left ventricular mass. Our study supports the findings of Liebson et al. (10) and Hammond et al. (11) in suggesting that in patients with established hypertension, the relation of left ventricular mass to age in hypertension is not independent of other predictors.

Limitations of the study. Most of our patients had received antihypertensive therapy before entry into the study; hence, our findings may not be applicable to hypertensive patients who have never been treated. Left ventricular mass did not differ between our treated and untreated patients but was inversely related to the number of medications used by treated patients. We therefore conclude that if these patients had not been given antihypertensive therapy, they would have had a higher left ventricular mass and that both average left ventricular mass and the prevalence of left ventricular hypertrophy in the total cohort would have been greater.

Clinical implications. The substantial benefit of decreasing blood pressure in hypertension is uncontested. However, both obesity and left ventricular hypertrophy contribute independently, and to a major degree, to cardiovascular risk. The additive and interactive contributions of obesity and systolic blood pressure to left ventricular hypertrophy suggest a mechanism for enhanced risk. Moreover, weight loss might reduce that risk by inducing regression of left ventricular hypertrophy, independently of additional beneficial effects on reduction of blood pressure.

Perhaps surprisingly, in light of published ECG studies, left ventricular mass and left ventricular hypertrophy prevalence were not greater in black than in white hypertensive men. However, the greater relative wall thickness in blacks, as well as increased septal and posterior free wall thickness, suggest an independent effect of race on the cardiac response to hypertension. Because increased relative wall thickness in itself confers increased cardiovascular risk, with and without the presence of left ventricular hypertrophy (3), the presence of concomitant obesity may have particularly severe implications for the cardiac risks of hypertension in black men.

References

1. Casale PN, Devereux RB, Milner M. Value of echocardiographic measurement of left ventricular mass in predicting cardiovascular morbid events in hypertensive men. Ann Intern Med 1986;105:173–8.
2. Levy D, Garrison RH, Savage DD. Prognostic implications of echocardiographically determined left ventricular mass in the Framingham Heart Study. N Engl J Med 1990;322:1561–6.
3. Koren MJ, Devereux RB, Casale PN. Relation of left ventricular mass and geometry to morbidity and mortality in uncomplicated essential hypertension. Ann Intern Med 1991;114:345–52.
4. Kannel WB, Dannenberg AL. Prevalance and natural history of electrocardiographic left ventricular hypertrophy. In: Messerli FH, editor. The Heart and Hypertension. New York: Yorke Medical Books, 1987;53–62.
5. Levy D, Anderson KM, Savage DD, Kannel WB, Christiansen JC, Castelli WP. Echocardiographically detected left ventricular hypertrophy: prevalence and risk factors. The Framingham Heart Study. Ann Intern Med 1988;108:7–13.
6. Egan B, Fitzpatrick MA, Juni J, Buda AJ, Zweifler A. Importance of overweight in studies of left ventricular hypertrophy and diastolic function in mild systemic hypertension. Am J Cardiol 1989;64:752–5.
7. Messerli FH, Nunez BD, Ventura HO, Snyder DW. Overweight and sudden death: increased ventricular ectopy in cardiopathy of obesity. Arch Intern Med 1987;147:1725–8.
8. Messerli FH, Sungaard-Riise K, Reisin ED, et al. Dimorphic cardiac adaptation to obesity and arterial hypertension. Ann Intern Med 1983;99:757–61.
9. Lauer MS, Anderson KM, Kannel WB, Levy D. Separate and joint influences of obesity and mild hypertension of left ventricular mass and geometry: the Framingham Heart Study. J Am Coll Cardiol 1992;19:130–4.
10. Liebson PR, Grandits G, Prineas R, et al. Echocardiographic correlates of left ventricular structure among 844 mildly hypertensive men and women in the treatment of mild hypertension study (TOMHS). Circulation 1993;87:476–86.
11. Hammond IW, Alderman MH, Devereux RB, Lutas EM, Laragh JH. Contrast in cardiac anatomy and function between black and white patients with hypertension. J Natl Med Assoc 1984;76:247–55.
12. Dannenberg AL, Levy D, Garrison RJ. Impact of age on echocardiographic left ventricular mass in a healthy population (the Framingham Study). Am J Cardiol 1989;64:1066–8.
13. Savage DD, Levy D, Dannenberg AL, Garrison RJ, Castelli WP. Association of echocardiographic left ventricular mass with body size, blood pressure and physical activity (the Framingham Study). Am J Cardiol 1990;65:371–6.
14. Koren MJ, Mensah GA, Blake J, Laragh JH, Devereux RB. Comparison of left ventricular mass and geometry in black and white patients with essential hypertension. Am J Hypertens 1993;6:815–23.
15. Sasson Z, Rasooly Y, Bhesania T, Rasooly I. Insulin resistance is an important determinant of left ventricular mass in the obese. Circulation 1993;88:1431–6.
16. Dahlof B. Factors involved in the pathogenesis of hypertensive cardiovascular hypertrophy. A review. Drugs 1988;35: Suppl 5:6–26.
17. Materson BS, Reda DJ, Cushman WC, et al. Monotherapy of hypertension: a multicenter trial of six drugs and placebo. N Engl J Med 1993;328:914–21.
18. Sahn DJ, DeMaria A, Kisslo J, Weyman A. The Committee on M-mode Standardization of the American Society of Echocardiography. Recommendations regarding quantitation in M-mode echocardiography: results of a survey of echocardiographic measurements. Circulation 1978;58:1072–83.
19. Troy BL, Pombo J, Rackley CE. Measurement of left ventricular wall thickness and mass by echocardiography. Circulation 1972;45:602–11.
20. Devereux RB, Lutas EM, Casale PN. Standardization of M-mode echocardiographic left ventricular anatomic measurements. J Am Coll Cardiol 1984;4:1222–30.
21. Boothby WM, Sandiford RB. Nomographic charts for the calculation of the metabolic rate by the gasometer method. Boston Med Surg J 1921;185:337–54.
22. Levy D, Savage DD, Garrison RJ, Anderson KM, Kannel WB, Castelli WP. Echocardiographic criteria for left ventricular hypertrophy: the Framingham Heart Study. Am J Cardiol 1987;59:956–60.
23. Savage DD, Garrison RJ, Kannel WB. The spectrum of left ventricular hypertrophy in general population sample: the Framingham Study. Circulation 1987;75:126–33.
24. Ganau A, Devereux RB, Roman MJ, et al. Patterns of left ventricular hypertrophy and geometric remodeling in essential hypertension. J Am Coll Cardiol 1992;19:1550–8.
25. Reichek N, Wilson J, St. John Sutton M, Plappert T, Goldberg S, Hirshfield J. Noninvasive determination of left ventricular end-systolic stress: validation of the method and initial application. Circulation 1982;65:99–108.
26. Grossman W, Braunwald E, Mann T, McLaurin LP, Green LH. Contractile state of the left ventricle in man as estimated from end-systolic pressure-volume relations. Circulation 1977;55:613–8.

27. Haffner SM, Stern MP, Hazuda HP, Pugh J, Patterson JK, Malina R. Upper body and centralized adiposity in Mexican Americans and non-Hispanic whites: relationship to body mass index and other behavioral and demographic variables. Int J Obes 1986;10:493–502.

28. Van Itallie TB. Health implications of overweight and obesity in the United States. Ann Intern Med 1985;103:983–8.

29. SAS/STAT users guide, version 6. Cary (NC): SAS Institute, 1989.

30. Woolson RF. Statistical Methods for the Analysis of Biomedical Data. New York: John Wiley, 1987:422–4.

31. Hammond IW, Devereux RB, Alderman MH, Laragh JH. Relation of blood pressure and body build to left ventricular mass in normotensive and hypertensive employed adults. J Am Coll Cardiol 1988;12:996–1004.

32. Hypertension Detection and Follow-Up Program Cooperative Group (HDFP). Race, education and prevalence of hypertension. Am J Epidemiol 1977;106:351–61.

33. Freis ED. Age, race, sex and other indices of risk in hypertension. Am J Med 1973;55:275–80.

34. Lee DK, Marantz PR, Devereux RB, Kligfield P, Alderman MH. Left ventricular hypertrophy in black and white hypertensives. Standard electrocardiographic criteria overestimate racial differences in prevalence. JAMA 1992;267:3294–9.

35. Dunn FG, Oigman W, Sungaard-Riise K. Racial differences in cardiac adaptation to essential hypertension determined by echocardiographic indexes. J Am Coll Cardiol 1983;1:1348–51.

36. Savage DD, Henry WL, Mitchell JR, et al. Echocardiographic comparison of black and white hypertensive subjects. JAMA 1979;71:709–12.

37. Pearson AC, Gudipati C, Nagelhout D, Sear J, Cohen JD, Labovitz AJ. Echocardiographic evaluation of cardiac structure and function in elderly subjects with isolated systolic hypertension. J Am Coll Cardiol 1991;17:422–30.