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Influence of Contemporary Versus 30-Year Blood Pressure Levels on Left Ventricular Mass and Geometry: The Framingham Heart Study

MICHAEL S. LAUER, MD, KEAVEN M. ANDERSON, PhD,* DANIEL LEVY, MD, FACC*

Boston and Framingham, Massachusetts

To determine whether long-term blood pressure levels correlate with left ventricular mass, echocardiographic measurements were performed in 152 men and 299 women who were participants in the Framingham Heart Study. All subjects were free of obesity and cardiovascular and pulmonary disease, were not taking antihypertensive medications and had echocardiographic studies that were adequate for estimating left ventricular mass.

Thirty-year average systolic blood pressure was correlated with left ventricular mass (corrected for height) (r = 0.27, p < 0.001 in men; r = 0.31, p < 0.001 in women). Multivariate linear regression analyses taking into account age and body mass index showed 30-year average systolic blood pressure to be a significant independent predictor of left ventricular mass (p < 0.01 in men and women). Systolic blood pressure at echocardiography was not independently associated with left ventricular mass when 30-year systolic blood pressure was entered into the multivariate model.

The prevalence of left ventricular hypertrophy was associated with 30-year average systolic blood pressure (odds ratio for every 20-mm Hg increase in blood pressure: 3.20, p < 0.05 in men; 3.27, p < 0.001 in women). The increase in left ventricular mass associated with 30-year average systolic blood pressure reflected changes in left ventricular wall thickness but not in left ventricular internal dimension. Thirty-year average diastolic blood pressure was also correlated with left ventricular mass but to a lesser degree than was systolic blood pressure (r = 0.18, p < 0.05 in men; r = 0.18, p < 0.01 in women).

It is concluded that long-term blood pressure levels are correlated with left ventricular mass and wall thickness but not with left ventricular internal dimension. Thirty-year average systolic blood pressure is a better predictor of left ventricular mass and wall thickness than is current rest blood pressure. Both current and long-term systolic blood pressures are better predictors of left ventricular mass and wall thickness than are current and long-term values for diastolic blood pressure.

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Left ventricular hypertrophy detected by electrocardiography and echocardiography has been shown to be an independent predictor of subsequent cardiovascular mortality and morbidity (1–4). In the Framingham Heart Study (5), echocardiographic left ventricular hypertrophy has been shown to be a common finding, with a prevalence rate of 15% to 20% in an adult population. Correlates and potential determinants of left ventricular mass have been described in the Framingham and other selected population groups (5–10). Attention has primarily focused on blood pressure, age, coronary and valvular heart disease and measures of body size.

Several cross-sectional studies (5,7,10) have shown an association of echocardiographically determined left ventricular mass with systemic arterial pressure. However, there have been no reports on how long-term systemic blood pressure trends in humans relate to the prevalence of left ventricular hypertrophy or to the differential relation among long-term blood pressure, wall thickness and left ventricular chamber size.

Using echocardiography, a sensitive noninvasive technique for the measurement of left ventricular mass (11–14), we sought in this study to examine the associations of echocardiographically determined left ventricular mass, wall thickness and chamber size with long-term measures of blood pressure in apparently healthy subjects in the Framingham Heart Study.

Methods

Study population. In 1948, a sample of the residents of Framingham, Massachusetts between the ages of 30 and 62 years was selected to undergo biennial examinations in a prospective epidemiologic study. Study design and selection criteria for the original Framingham population-based sample have been described previously (15–18). Clinical examinations included measurements of blood pressure, height and weight. Informed consent was obtained from all subjects before the study.

To be eligible for this study, subjects had to meet the

From the Charles A. Dana Research Institute and Harvard-Thorndike Laboratory, Department of Medicine, Cardiovascular Division, Beth Israel Hospital and Harvard Medical School, Boston and the *Framingham Heart Study of the National Heart, Lung, and Blood Institute, Framingham, Massachusetts. This study was supported by Grant HL07374 under Contract NO1-HC-38038 from the National Institutes of Health, Bethesda, Maryland.

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Address for reprints: Daniel Levy, MD, Framingham Heart Study, 5 Thurber Street, Framingham, Massachusetts 01701.

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following conditions: 1) no history or clinical evidence of coronary heart disease (including myocardial infarction, coronary insufficiency and angina pectoris), congestive heart failure, pulmonary disease or valvular heart disease; 2) no receipt of drug treatment for hypertension; 3) weight neither >30% above nor >10% below the midpoint of recommended weight (medium build range) for that height in the 1959 Metropolitan Life Insurance Company tables; and 4) echocardiograms of adequate quality to estimate left ventricular mass.

Myocardial infarction, coronary insufficiency, congestive heart failure and pulmonary disease were diagnosed on review of clinical history, electrocardiographic and chest X-ray findings and hospitalization records. The presence of angina pectoris was determined on the basis of clinical history obtained by two examining physicians, with discrepancies arbitrated by a review committee of three physicians. The diagnosis of valvular disease was based on clinical evidence of a grade ≥3/6 systolic murmur or any diastolic murmur or echocardiographic evidence of left-sided valvular disease exclusive of mitral valve prolapse.

Blood pressure measurements. At each biennial examination, systolic and diastolic blood pressure were measured in the left arm with a mercury column sphygmomanometer while the subject was seated. At each examination the measurements were obtained by two physicians and the values averaged to derive the respective *examination* systolic or diastolic pressure. The *index examination* was that performed at the time echocardiography was performed.

The following systolic and diastolic blood pressure variables were studied as potential correlates of left ventricular mass: 1) systolic and diastolic pressure at the index examination, hereafter called index examination systolic or diastolic blood pressure; 2) average (mean) systolic and diastolic pressure over the 30-year study period obtained by averaging all examination blood pressure determinations available, hereafter called 30-year average systolic or diastolic blood pressure; and 3) the maximal observed examination systolic and diastolic blood pressure over the 30-year period, hereafter called maximal 30-year systolic or diastolic blood pressure.

Echocardiographic methods. From 1979 to 1983, M-mode echocardiography was performed on 2,291 of 2,351 surviving original Framingham Heart Study subjects undergoing their 16th biennial examination. Body height and weight measurements, as well as rest blood pressure, were obtained at the time of the echocardiographic examination.

Participants were studied in accordance with standard M-mode echocardiographic methods as previously reported (13,19–22). End-diastolic measurements of left ventricular chamber diameter (LVID), interventricular septum thickness (IVST) and posterior wall thickness (PWT) were obtained with use of both the American Society for Echocardiography and the Penn (13) conventions. Left ventricular mass (Penn) (LVM) in grams was calculated with the formula of Devereux et al. (23):

$$LVM = 1.04([LVID + PWT + IVST]^3 - [LVID]^3) - 13.6.$$

Left ventricular hypertrophy was defined as a left ventricular mass corrected for height ≥2 SD above the mean for a previously defined healthy reference group of 864 subjects (20). The cutoff values for echocardiographic left ventricular hypertrophy were 143 g/m in men and 102 g/m in women (20).

Wall thickness was calculated as the sum of the end-diastolic thicknesses of the interventricular septum and posterior wall.

Statistical methods. All analyses were gender specific. Unless otherwise stated, continuous variables were compared with a two-sided Student's *t* test. Pearson correlations were used to estimate and test the strengths of association between left ventricular mass and age, body mass index and various measures of systolic and diastolic blood pressure. Because strengths of association are partly affected by degrees of measurement error, the correlations between index examination blood pressures and left ventricular mass were adjusted upward, using the method of moments, in which measurement error estimated by the intraindividual SD for rest blood pressure was taken into account. Thus, the adjusted r value (r_{adj}) was calculated as follows:

$$r_{adj} = r \times (s_p/[s_p^2 - s_w^2/2]^{0.5}),$$

where s_p is the SD for index examination blood pressure in the study group and s_w is the intraindividual SD for that blood pressure variable. Further analyses estimated age-adjusted mean left ventricular mass for different levels of systolic blood pressure. The systolic blood pressure groups used were <120, 120 to 129, 130 to 139 and >140 mm Hg. Similar Pearson correlation coefficient and linear regression analyses were done to assess the associations of end-diastolic left ventricular internal diameter and wall thickness with various measures of blood pressure and blood pressure trends. With use of linear regression least squares analysis, age-adjusted increments in left ventricular mass were estimated for 1-SD increments in the various blood pressure levels.

Age-adjusted rates of left ventricular hypertrophy for different levels of systolic blood pressure were calculated with the direct method, using the same blood pressure groups used for left ventricular mass calculations. Age-adjusted left ventricular hypertrophy prevalence trends were tested with the generalized Cochran-Mantel-Haenszel statistic. Age-adjusted odds ratios of left ventricular hypertrophy for 1-SD increments in systolic and diastolic pressure were estimated with logistic regression analysis.

If an examination blood pressure value was missing, the corresponding blood pressure value obtained from the preceding examination or, if not available, the value from the subsequent examination was substituted.

In additional multivariate linear regression analyses, the relations among 30-year average systolic and diastolic pres-

Table 1. Derivation of the Study Subjects

	Men (no.)	Women (no.)
Reference population at examination 1	2,336	2,873
Exclusions		
1. Death before examination 16; no. remaining	−1,100:1,236	−902:1,971
2. Missed examination 16; no. remaining	−302:934	−554:1,417
3. Outside weight limits*; no. remaining	−259:675	−454:963
4. Congestive heart failure; no. remaining	−18:657	−31:932
5. Coronary heart disease; no. remaining	−203:454	−167:765
6. Valvular heart disease; no. remaining	−47:407	−69:696
7. Pulmonary disease; no. remaining	−67:340	−60:636
8. Cardiovascular medications; no. remaining	−106:234	−202:434
9. Inadequate echocardiogram; no. remaining	−82:152	−135:299

*Metropolitan relative weight >130 or <90.

Table 2. Clinical Characteristics of the Study Subjects

	Men (n = 152)	Women (n = 299)
Age (yr)	68 ± 6	68 ± 6
Weight (kg)	75 ± 8	60 ± 7
Height (cm)	171 ± 7	157 ± 7
Body mass index (kg/m²)	25 ± 2	24 ± 2
Blood pressure (mm Hg)		
Index systolic	135 ± 18	134 ± 20
Index diastolic	80 ± 8	75 ± 9
Maximal 30-yr systolic	144 ± 16	145 ± 18
Maximal 30-yr diastolic	89 ± 7	86 ± 8
30-yr average systolic	125 ± 10	123 ± 11
30-yr average diastolic	79 ± 6	75 ± 6
LV mass (Penn) (g)	192 ± 56	138 ± 40
LV mass/height (g/m)	112 ± 32	88 ± 25
Wall thickness (mm)	20 ± 3	18 ± 3
LVIDD (mm)	49 ± 4	44 ± 4

Data are mean values ± SD. LV = left ventricular; LVIDD = left ventricular internal dimension at end-diastole.

sure, maximal 30-year systolic and diastolic pressure and echocardiographic left ventricular variables were examined after adjusting for age and body mass index at the time of echocardiography.

Results

Selection of participants (Table 1). Of the 934 men and 1,417 women who underwent examination 16, 234 men and 434 women did not have pulmonary or cardiovascular disease and were not taking cardiovascular or antihypertensive medications. One hundred fifty-two (65%) of the eligible men and 299 (69%) of the eligible women had adequate echocardiographic studies. Subjects with suboptimal echocardiograms were older than were those with adequate echocardiographic studies (71 ± 7 vs. 67 ± 6 years [$p < 0.001$] among men and 71 ± 6 vs. 68 ± 6 years [$p < 0.001$] among women), but the two groups did not differ in body mass index or systolic or diastolic blood pressure.

Characteristics of participants (Table 2). At the time of echocardiographic study (index examination), the mean systolic blood pressure was 135 mm Hg in men and 134 mm Hg in women. The 30-year average systolic blood pressure was about 10 mm Hg lower than the index examination systolic blood pressure in both men and women ($p < 0.001$), whereas maximal 30-year systolic blood pressure was about 10 mm Hg higher ($p < 0.001$) than the index examination systolic blood pressure. The median interval between the observed maximal 30-year systolic blood pressure and the index examination was 6 years in both men and women; the maximal 30-year systolic blood pressure was obtained within 10 years of the index examination blood pressure in 75% of the participants. All of these observations are consistent with an increase in systolic blood pressure with age. Diastolic pressure, however, did not appear to change significantly with time.

Influence of different blood pressure variables on left ventricular mass (Tables 3 and 4). Pearson correlation coefficients suggest a moderate but highly significant association between both index examination systolic and diastolic pressure and left ventricular mass. Of note, 30-year average pressure and maximal 30-year pressure had a stronger association with left ventricular mass than did index examination blood pressure (Table 3).

All blood pressure variables, including index, 30-year average, maximal 30-year and 10-year previous blood pressures, were strongly correlated with one another. Therefore, to determine whether 30-year average, maximal and 10-year previous systolic blood pressures exercised effects on left ventricular mass beyond their associations with index examination systolic pressure (and age), multivariate linear regression analyses were carried out, controlling for age and index examination systolic blood pressure. After controlling for 1) 30-year average systolic and diastolic pressure, and 2) maximal 30-year systolic and diastolic blood pressure, the corresponding index examination blood pressure was no longer significantly associated with left ventricular mass.

The relations between different systolic blood pressure variables and age-adjusted left ventricular mass are illustrated in Figure 1 (for men) and Figure 2 (for women). Age-adjusted left ventricular mass increased with higher levels of index systolic blood pressure ($p < 0.05$ for men, $p < 0.01$ for women), maximal 30-year systolic blood pressure ($p < 0.05$ for men and women) and average 30-year systolic blood pressure ($p < 0.05$ for men, $p < 0.01$ for women).

Table 4 shows increments in left ventricular mass cor-

Table 3. Relation of Left Ventricular Mass, Wall Thickness and Diastolic Dimension to Age, Body Mass Index and Blood Pressure Variables

	Men			Women		
	LV Mass/ Height	SWT	LVIDD	LV Mass/ Height	SWT	LVIDD
Age	0.05	0.02	−0.08	0.28*	0.32*	−0.11
Body mass index	0.22†	0.21†	0.11	0.32*	0.21†	0.19†
Index SBP	0.23†	0.18‡	0.08	0.24*	0.24*	0.01
30-yr average SBP	0.27*	0.24†	0.1	0.31*	0.33*	−0.02
Maximal 30-yr SBP	0.3*	0.27*	0.08	0.33*	0.35*	−0.01
Index DBP	0.11	0.18‡	−0.03	0.05	0.1	−0.01
30-yr average DBP	0.18‡	0.23†	0.03	0.18†	0.23*	−0.04
Maximal 30-yr DBP	0.28*	0.3*	0.06	0.17†	0.22*	−0.04

*p < 0.001; †p < 0.01; ‡p < 0.05. Values shown are Pearson correlation coefficients. DBP and SBP = diastolic and systolic blood pressure, respectively; SWT = sum of wall thickness measurements (that is, sum of interventricular septal and posterior wall thickness measurements); other abbreviation as in Table 2.

rected for height as a function of 1-SD differences in blood pressure variables after adjusting for age and body mass index in multivariate linear regression analyses. For example, a 1-SD increase in index systolic blood pressure in men was associated with a 7-g/m increase in left ventricular mass/height ratio ($p < 0.01$), whereas in women, it was associated with a 4-g/m increase ($p < 0.01$). Left ventricular mass remained associated with 30-year average and maximal systolic blood pressure ($p < 0.01$ in men and women) but was not significantly associated with diastolic blood pressure variables.

Adding age, body mass index and 30-year average diastolic pressure to 30-year average systolic pressure in a linear model for left ventricular mass increased the multiple r value over that given in Table 3 from 0.27 to 0.32 in men ($p < 0.01$) and from 0.31 to 0.45 in women ($p < 0.001$).

Influence of blood pressure on wall thickness and left ventricular chamber size (Table 3). Wall thickness was significantly correlated with both systolic and, to a lesser extent, diastolic blood pressure variables, but no association was observed between end-diastolic left ventricular internal dimension and blood pressure. The impact of 30-year average systolic blood pressure on age-adjusted wall thickness is shown in Figure 3. Women with a 30-year average systolic pressure >140 mm Hg had a wall thickness 14% greater than that of women with an average systolic pressure <120 mm Hg ($p < 0.001$). Conversely, 30-year average systolic pressure had no association with age-adjusted end-diastolic left ventricular internal dimension ($p = 0.61$). Similar relations were seen for index examination and maximal 30-year systolic blood pressure. In men, age-adjusted wall thickness was also significantly increased with increasing levels of index, maximal 30-year and 30-year average systolic pressure (all $p < 0.05$). As with women, blood pressure variables were not observed to have an effect on end-diastolic left ventricular internal dimension.

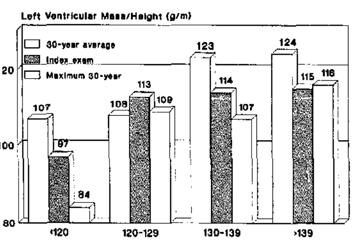
Although age-adjusted left ventricular mass was not associated with diastolic blood pressure variables, age-adjusted left ventricular wall thickness did increase with

Table 4. Age-Adjusted Increments for Left Ventricular Mass/Height (in g/m) as a Function of 1-SD Increments in Blood Pressure Variables*

Independent Variable	Men	Women
Index SBP	7†	4†
30-yr average SBP	8†	5†
Maximal 30-yr SBP	9‡	5‡
Index DBP	4§	2§
30-yr average DBP	5§	2§
Maximal 30-yr DBP	7†	2§

*Results of linear regression analysis adjusting for age and body mass index. †p < 0.01; ‡p < 0.001; §p = NS. Values shown are left ventricular mass estimates for the 1-SD increments of the independent variables. Abbreviations as in Table 3.

Figure 1. Age-adjusted left ventricular mass corrected for height in men, according to systolic blood pressure variables. Mean left ventricular mass/height ratios corresponding to 30-year average systolic blood pressure are represented by the **white bars** ($p < 0.05$), those for the index examination (exam) systolic blood pressure by the **hatched bars** ($p < 0.05$) and maximal 30-year systolic blood pressure by the **stippled bars** ($p < 0.05$).



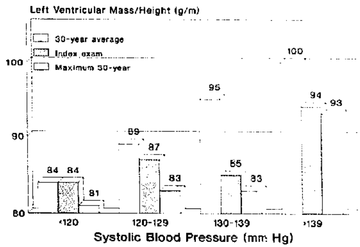


Figure 2. Age-adjusted left ventricular mass corrected for height in women, according to systolic blood pressure variables. Mean left ventricular mass/height ratios corresponding to 30-year average systolic blood pressure are represented by the **white bars** ($p < 0.01$), those for the index examination (exam) systolic blood pressure by the **hatched bars** ($p < 0.01$) and maximal 30-year systolic blood pressure by the **stippled bars** ($p < 0.05$).

increasing index diastolic blood pressure ($p < 0.05$ in men and women) as well as maximal 30-year ($p < 0.001$ in men and women) and 30-year average ($p < 0.01$ in men and women) diastolic blood pressure.

Prevalence of left ventricular hypertrophy (Table 5). Left ventricular mass/height criteria for left ventricular hypertrophy were met in 21 men and 61 women, yielding a prevalence rate of 13.7% and 20.4%, respectively. Age-adjusted prevalence rates of left ventricular hypertrophy for different blood pressure groups are shown in Figure 4. Among women, the age-adjusted prevalence rate of left ventricular hypertrophy ranged from 14% for 30-year average systolic pressure <120 mm Hg to 33% for pressure >140 mm Hg ($p = 0.01$). Similarly, in women, the age-adjusted prevalence rate of left

Table 5. Age-Adjusted Odds Ratios for Prevalence of Left Ventricular Hypertrophy as a Function of 1-SD Increments in Blood Pressure Variables*

Independent Variable	Men	Women
Index SBP	1.27†	1.69‡
30-yr average SBP	1.76§	1.87‡
Maximal 30-yr SBP	1.65§	1.97‡
Index DBP	1.01†	1.34§
30-year average DBP	1.36†	1.66‖
Maximal 30-year DBP	1.77§	1.37§

*Results of logistic regression analysis adjusting for age and body mass index. Odds ratios are computed from logistic regression coefficients. †p = NS; ‡p < 0.001; §p < 0.05; ‖p < 0.01. Values shown are odds ratio estimates for the 1-SD increments of the independent variables. Abbreviations as in Table 3.

ventricular hypertrophy ranged from 9% for maximal 30-year systolic pressure <120 mm Hg to 28% for 30-year pressure >140 mm Hg. Similar trends were observed among men, but they did not reach statistical significance, owing to the small number of men with left ventricular hypertrophy.

As was observed in the left ventricular mass analyses, index examination systolic and diastolic pressure had no relation to the left ventricular hypertrophy prevalence rate when other long-term blood pressure variables were considered concomitantly with use of multivariate logistic regression analysis.

Table 5 shows odds ratios for the prevalence of left ventricular hypertrophy as a function of different blood pressure variables after adjusting for age and body mass index in multivariate logistic regression analyses. The changes in blood pressure variables correspond to 1-SD differences for the study subjects. Thus, a 1-SD increase in 30-year average systolic blood pressure was associated with an odds ratio for left ventricular hypertrophy of 1.76 in men ($p < 0.05$) and 1.87 in women ($p < 0.001$). The odds ratio for

Figure 3. Age-adjusted left ventricular wall thickness according to levels of 30-year average systolic blood pressure. Wall thickness values for men are represented by the **white bars** ($p < 0.05$) and those for women by the **hatched bars** ($p < 0.001$).

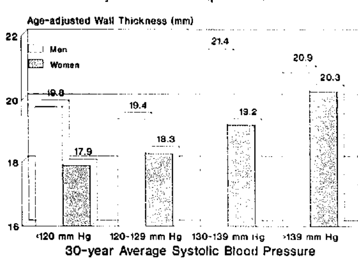
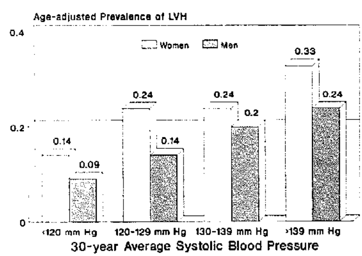


Figure 4. Age-adjusted prevalence rates of left ventricular hypertrophy (LVH) according to levels of 30-year average systolic blood pressure. Prevalence rates for women are represented by the **white bars** ($p = 0.01$) and those for men by the **hatched bars** (p = NS).



left ventricular hypertrophy was 3.20 ($p < 0.05$) and 3.27 ($p < 0.001$) for a 20-mm Hg increase in 30-year average systolic blood pressure in men and women, respectively. The relation between left ventricular hypertrophy and 30-year average diastolic blood pressure was less marked (for a 1-SD increase in 30-year average diastolic blood pressure, the odds ratio for left ventricular hypertrophy was 1.36 [p = NS] in men and 1.66 [$p < 0.01$] in women).

Effects of correcting for height. As mentioned, left ventricular mass values were corrected for height instead of body surface area because previous work at Framingham (5) suggested that correcting for body surface area fails to identify left ventricular hypertrophy in obese persons. When analyses were carried out by correcting left ventricular mass for body surface area (instead of for height), there were no substantial changes in any of the blood pressure analyses; no correlation coefficient changed by >0.01. As expected, however, the observed associations between body mass index and left ventricular mass did significantly weaken (from $r = 0.22$ [$p < 0.01$] to $r = 0.11$ in men [$p > 0.10$]; from $r = 0.32$ [$p < 0.001$] to $r = 0.20$ [$p < 0.001$] in women).

Effects of adjusting for body mass index. Body mass index was positively associated with left ventricular mass, left ventricular wall thickness and left ventricular internal dimension (Table 3). Body mass index was also associated with 30-year average systolic blood pressure ($r = 0.20$, $p < 0.05$ in men; $r = 0.17$, $p < 0.01$ in women) and 30-year average diastolic blood pressure ($r = 0.29$, $p < 0.001$ in men; $r = 0.23$, $p < 0.001$ in women). Therefore, multivariate linear regression analyses were performed to assess the influences of blood pressure variables after adjusting for body mass index (and age). Average and maximal 30-year systolic blood pressure remained significantly associated with left ventricular mass corrected for height ($p < 0.01$ in men and women) and with left ventricular wall thickness ($p \leq 0.01$ in men and women). Thirty-year average diastolic blood pressure was not significantly associated with left ventricular mass after adjusting for body mass index; however, it was still significantly associated with left ventricular wall thickness ($p < 0.05$ in men; $p < 0.01$ in women). Similarly, maximal 30-year diastolic blood pressure remained significantly associated with left ventricular wall thickness ($p < 0.01$ in men and women).

Discussion

Principal findings. Previous work from Framingham (9) and elsewhere (4,7,12) has shown an association between measurements of rest blood pressure and left ventricular mass. The present study extends our understanding of the blood pressure-left ventricular mass relation by demonstrating that left ventricular mass is related to long-term trends in blood pressure to a greater extent than are concurrent levels at rest and that this association primarily reflects changes in left ventricular wall thickness rather than left ventricular chamber size.

Systolic blood pressure at rest at the time of the index examination correlated only moderately with left ventricular mass in our study subjects. The relatively low degree of correlation observed ($r = 0.22$ in men; $r = 0.23$ in women) is similar to that observed by other investigators (23–25). There was no observed relation between rest diastolic blood pressure at the index examination and left ventricular mass. Some investigators (24) also reported no association of diastolic pressure with left ventricular mass, whereas others (23,25) noted a weak relation.

Reasons for poor correlations between blood pressure at rest and left ventricular mass. One reason why the observed correlation coefficients relating blood pressure at rest to left ventricular mass were relatively small may be the restricted nature of the study group. Because subjects with obesity and coronary heart disease, as well as those receiving drug treatment for hypertension, were excluded, the range of blood pressure values among the participants was small. Twenty-one men (14%) and 52 women (17%) had either a systolic blood pressure >160 mm Hg or a diastolic blood pressure >95 mm Hg at the index examination. Only 1% of the men studied and none of the women studied had a 30-year average systolic blood pressure >160 mm Hg.

To better understand the nature of the association between blood pressure and left ventricular mass, investigators have considered blood pressure variables other than clinical values at rest. Devereux et al. (25) performed echocardiography and ambulatory blood pressure monitoring in 19 normal subjects and 81 patients with mild hypertension. They also noted a weak correlation between systolic blood pressure at rest and left ventricular mass ($r = 0.24$, $p < 0.05$). The ambulatory blood pressure variable with the strongest association with left ventricular mass was average systolic pressure during exercise ($r = 0.50$, $p < 0.001$); exercise diastolic pressure was also correlated with left ventricular mass but to a lesser extent ($r = 0.39$, $p < 0.001$) (25). Another potential blood pressure correlate with left ventricular mass is peak systolic blood pressure during exercise. Case comparison studies of small numbers of normotensive men (26), hypertensive patients (27) and ultraendurance athletes (28) reported strong associations between exercise systolic blood pressure and echocardiographic left ventricular mass.

All of the blood pressure variables just mentioned reflect short-term associations between blood pressure and left ventricular mass; the present study considered long-term blood pressure trends obtained over 30 years. The maximal 30-year blood pressure, which occurred at a median interval of 6 years before the time of echocardiographic study, also correlated with left ventricular mass. Of note, the degree of correlation between average or maximal systolic blood pressure and left ventricular mass was greater than that of systolic blood pressure obtained at the time of echocardiography. Also, 30-year average and maximal 30-year diastolic pressures were correlated with left ventricular mass (unlike the index examination diastolic pressure), but to a slightly lesser extent than were the corresponding systolic blood pressure variables. These observations support the hypothesis that the duration and severity of elevated blood pressure promote left ventricular hypertrophy. They also suggest that systolic blood pressure is at least as important in the promotion of left ventricular hypertrophy as is diastolic blood pressure.

Long-term blood pressure and left ventricular mass. One possible reason why average 30-year blood pressure correlated better with left ventricular mass than did index examination blood pressure is that the former was derived from many more blood pressure measurements and consequently had lower SD values. Thus, the greater degrees of correlation may merely represent decreased measurement error or a regression toward the mean value. However, the correlation differences persisted when index examination blood pressure correlations were adjusted by taking into account intraindividual SD values for rest blood pressures. In fact, the upward adjustments in Pearson correlation coefficients for index examination systolic and diastolic pressure were minimal (2.5% and 4%, respectively). Also, the maximal 30-year systolic blood pressure had an SD similar to that of the index examination systolic blood pressure but was more highly correlated with left ventricular mass. Finally, in multiple linear regression analysis, when 30-year average systolic blood pressure was entered into the model, the relation between systolic blood pressure at the index examination and left ventricular mass was no longer statistically significant.

The absolute relations between long-term blood pressure and left ventricular mass were quite marked. For example, for every 20-mm Hg increase in 30-year average systolic blood pressure, the prevalence of left ventricular hypertrophy increased more than threefold in both men and women. Also, increasing levels of blood pressure considered to be within the currently accepted normal range had a sizable impact on left ventricular mass (Fig. 1) and increased the risk of left ventricular hypertrophy (Fig. 4).

Differential effects of blood pressure on wall thickness and chamber size. A notable finding of this study is the differential effects of blood pressure on left ventricular wall thickness and chamber size. Previous work by Savage et al. (12) comparing hypertensive subjects (many taking medications) and nonhypertensive control subjects showed abnormally increased free wall thickness in 61% of the hypertensive subjects but an abnormal end-diastolic left ventricular internal dimension in only 5%. In the present study, associations of blood pressure with left ventricular wall thickness in a healthy, nonmedicated general population sample were parallel with associations with left ventricular mass (Fig. 3). Subjects with 30-year average systolic blood pressure >140 mm Hg had a 5% (in men) to 20% (in women) increase in wall thickness compared with those with a 30-year average systolic blood pressure <120 mm Hg. Blood pressure had no relation, however, to end-diastolic left ventricular internal dimension. These observations support the hypothesis that increasing blood pressure increases left ventricular mass by increasing wall thickness without affecting left ventricular chamber size.

Previously, Grossman et al. (29) studied six normal subjects and six subjects with a pressure-overloaded left ventricle; the pressure-overloaded ventricles had markedly thickened free walls (15.2 ± 9 vs. 8.2 ± 6 mm, $p < 0.01$). A similar pattern of marked left ventricular wall thickening, although with decreased chamber size, was observed (30) among a subset of elderly hypertensive patients with a recently described form of hypertrophic cardiomyopathy. Both of these studies support the hypothesis that pressure-related left ventricular hypertrophy primarily reflects an increase in left ventricular wall thickness; this may be at the expense of left ventricular chamber size in some individuals. It has been proposed (29) that peak systolic wall stress is a key stimulus to the development of left ventricular hypertrophy, which may explain why systolic blood pressure is more closely correlated with left ventricular mass and wall thickness than is diastolic blood pressure.

Limitations. The present study has several limitations. The study group was restricted to exclude subjects with obesity, pulmonary and cardiovascular disease and treated hypertension. Although these exclusions allow for less confounding of analyses than otherwise, the relations between long-term blood pressure variables and left ventricular mass or geometry may be different in patients with cardiovascular disease or obesity. Because subjects with diastolic hypertension may have been more likely to receive drug treatment than those with primarily systolic hypertension, the observed effects of diastolic blood pressure may have been attenuated. Finally, the Framingham cohort is overwhelmingly white and thus the study may not correctly describe blood pressure-left ventricular mass relations in blacks.

Implications. It is well established that left ventricular hypertrophy is an independent cardiovascular risk factor (1–4). The pathophysiologic mechanisms involved are incompletely understood; they may include increased myocardial oxygen demand, decreased coronary flow reserve, increased susceptibility to ventricular arrhythmias or combinations of these factors (3). In any case, treatment of hypertension in elderly patients has been demonstrated to promote regression of left ventricular hypertrophy and improve hemodynamics (31). This recent finding (31) suggests at least two major potential clinical implications of the present study. First, because even small elevations of long-term systolic blood pressure are associated with an increase in left ventricular mass, our thresholds for intervention in hypertension may need to be lowered if we seek to prevent the development of left ventricular hypertrophy. Second, because increases in left ventricular mass and wall thickness are associated with long-term systolic blood pressure to at least as great a degree as long-term diastolic blood pressure, this study suggests that persons with isolated systolic hypertension, an entity quite common in the elderly, may benefit from more aggressive management. Prospective clinical studies will be needed to further address these questions.

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