Echocardiographically Detected Left Ventricular Hypertrophy: Prevalence and Risk Factors

The Framingham Heart Study

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The prevalence of and risk factors associated with echocardiographically determined left ventricular hypertrophy were examined in 4976 participants in the Framingham Heart Study (age, 17 to 90 years). Left ventricular hypertrophy was detected in 356 men (16%) and 513 women (19%). Prevalence increases dramatically with age ($P < 0.001$), with 33% of men and 49% of women age 70 or older affected. A significant association between blood pressure and left ventricular hypertrophy is present and occurs at levels of systolic pressure below 140 mm Hg (age adjusted, $P < 0.001$). There is a ninefold (women) to tenfold (men) increase from leanest to most obese group (age adjusted, $P < 0.001$). In multivariate analysis, age, blood pressure, obesity, valve disease, and myocardial infarction are independently associated in both sexes. We conclude that left ventricular hypertrophy is a common echocardiographic finding for which several risk factors can be identified. These findings support weight reduction and blood pressure control for prevention or regression of this condition.

In the Framingham Study left ventricular hypertrophy detected by electrocardiography has long been recognized as a consequence of hypertension as well as an independent predictor of subsequent cardiovascular morbidity and mortality (1-4). The advent of echocardiography has made possible the noninvasive estimation of left ventricular mass (5-9). Autopsy studies have confirmed the validity of in-vivo echocardiographic estimates of left ventricular mass (7-9).

Comparison studies have shown that echocardiography is far more sensitive than electrocardiography for detecting increases in left ventricular mass (6, 10). Electrocardiographic evidence of left ventricular hypertrophy was found in 3.2% of Framingham Study participants age 30 to 62 (2) and in 5% of hypertensive subjects of the Hypertension Detection and Follow-up Program (11). These estimates are lower than those obtained by echocardiography. Available estimates of the prevalence of echocardiographic left ventricular hypertrophy are limited to hypertensive populations and workplace-based reports, but suggest prevalence rates of 3% in normotensive subjects and 25% to 30% in hypertensive patients (12-14). To date, little is known about the prevalence of echocardiographic left ventricular hypertrophy in the general population.

Not only has echocardiography been established as an accurate noninvasive method for detection of left ventricular hypertrophy, but preliminary data have also implicated echocardiographic left ventricular hypertrophy as a potent predictor of cardiovascular morbidity (15) and mortality (16).

The introduction of echocardiography into clinical and epidemiologic settings has permitted the development of new criteria for diagnosis of left ventricular hypertrophy (7, 17). By applying these reference criteria to the general population one can estimate the prevalence of echocardiographic left ventricular hypertrophy and examine the contributory roles of age, blood pressure, obesity, and coronary and valvular heart disease.

The present study reports the prevalence and the potential determinants of echocardiographically determined left ventricular hypertrophy in participants in the Framingham Heart Study.

Methods

STUDY POPULATION

In 1948, 5209 residents of Framingham, Massachusetts, between the ages of 28 and 62 were selected to undergo biennial examinations in a prospective epidemiologic study. Offspring of the original cohort (and their spouses) were entered into the study in 1972. Selection criteria and study design have been reviewed previously (18-21). From 1979 to 1983, echocardiograms were done on 2291 of 2351 surviving original cohort subjects undergoing their sixteenth biennial examination, and on 3857 of 3867 offspring undergoing their second examination. Body height and weight measurements, as well as resting blood pressure measurements, were obtained at the time of the echocardiographic examination. Body surface area was calculated from the formula (22): body surface area (m^2) = $(0.0001) \times (71.84) \times (\text{weight in kg})^{0.425} \times (\text{height in cm})^{0.725}$.

ECHOCARDIOGRAPHIC METHODS

Participants were studied in accordance with standard M-mode echocardiographic methods as previously reported (17). In more than 90% of participants, two-dimensional imaging (23) was done to aid interpretation of the M-mode studies. Measurements were made according to the recommendations of the American Society of Echocardiography and used a leading edge to leading edge convention (24). The left ventricular internal dimension, interventricular septum, and left ventricular posterior wall were measured at end diastole as defined by the onset of the QRS complex. Each of these structures had to be

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measurable for the study to be considered adequate. Left ventricular mass was calculated from the formula of Troy and associates (5):

Left ventricular mass (g) = 1.05 ([left ventricular internal diameter + ventricular septal thickness + posterior wall thickness]) cubed − [(left ventricular internal diameter] cubed).

To generate normative reference data, a healthy subset of 864 study participants, ages 18 to 79, was derived (17). Healthy participants were free of any history or clinical evidence of cardiovascular or pulmonary disease, hypertension, or obesity, and were not taking any cardiac or antihypertension medication. Criteria for upper limits of normal left ventricular mass based on mean values plus two standard deviations for left ventricular mass, left ventricular mass/body surface area, and left ventricular mass/height are respectively: 294 g, 150 g/m^2, and 163 g/m in men; and 194 g, 120g/m^2, and 121 g/m in women. These reference criteria were then applied to the entire study population to determine the prevalence of echocardiographic left ventricular hypertrophy. Because of the widespread use of American Society of Echocardiography methods, results using this convention are presented in this paper; however, left ventricular mass values obtained with this approach have been found to overestimate anatomical mass by approximately 20% (9). Corresponding values based on the "Penn" convention measurements and formula (8) are provided for reference purposes. Upper limits of normal for "Penn" left ventricular mass, left ventricular mass/body surface area, and left ventricular mass/height are respectively: 259 g, 131 g/m^2, and 143 g/m in men; and 166 g, 100 g/m^2, and 102 g/m in women.

STATISTICAL METHODS

Linear regression analyses were used to compute age-adjusted characteristics of subjects. A linear regression model was used to adjust for age and to test for differences between subjects with echocardiograms of adequate quality to calculate left ventricular mass and those subjects with technically inadequate studies.

Age-adjusted rates of left ventricular hypertrophy were calculated using the direct method. The age groups used were under 30 years, 30 to 39, 40 to 49, 50 to 59, 60 to 69, and/or over 70. Left ventricular hypertrophy prevalence trends were tested with the generalized Cochran-Mantel-Haenszel statistic.

Multiple logistic analyses were used to test the association of systolic blood pressure, antihypertension drug therapy, body mass index, myocardial infarction, angina pectoris, and valve disease with occurrence of left ventricular hypertrophy. Myocardial infarction was diagnosed on review of clinical history, electrocardiographic findings, and hospitalization records. Angina pectoris was determined on the basis of clinical history obtained by two examining physicians with discrepancies arbitrated by a three-physician review committee. The diagnosis of valve disease was based on clinical examination evidence of a grade $\geq$ III/VI intensity systolic murmur, or any diastolic murmur, or echocardiographic evidence of left-sided valvular disease exclusive of mitral valve prolapse. Dichotomous variables were given a value of 0 if absent, or 1 if present. A stepwise procedure with an entry level P value of 0.05 was used for variable selection. The multiple logistic regression coefficients were used to compute odds ratios for prevalence of left ventricular hypertrophy based on increments of the various risk factors studied. Estimates of risk for left ventricular hypertrophy, for the various risk factors, are based on multiple logistic odds ratios.

Results

CHARACTERISTICS OF PARTICIPANTS

M-mode echocardiographic studies of adequate quality to permit calculation of left ventricular mass were obtained in 4976 (81%) of 6148 participants in whom studies were attempted. Those without adequate echocardiograms were older and more obese ($P < 0.001$), but did not have higher blood pressure, or higher rates of smoking or coronary disease, than those with adequate studies. In men, the mean age was 50 years for subjects with adequate studies and 65 for those with suboptimal studies. Corresponding values in women were 52 and 69 years, respectively. In both sexes, mean body mass index was 1 kg/m^2 greater in subjects with inadequate compared to those with adequate echocardiograms. Among participants with adequate echocardiograms, the age-specific rates of hypertension, myocardial infarction, angina pectoris and valve disease are shown in Table 1.

CRITERIA FOR ECHOCARDIOGRAPHIC LEFT VENTRICULAR HYPERTROPHY

When the age-adjusted prevalence of left ventricular hypertrophy is examined according to height, a significant, and presumably undesirable, trend ($P < 0.001$) toward increased rates of left ventricular hypertrophy in taller participants emerges when left ventricular mass criteria are used that do not adjust for body size. This finding suggests a need for left ventricular hypertrophy criteria that correct left ventricular mass by a measure of body size. One approach is to adjust left ventricular mass by body surface area. This strategy has the disadvantage of allowing obese persons higher thresholds of left ventricular mass before left ventricular mass/body surface area criteria for left ventricular hypertrophy are reached. No such "forgiveness" of obesity occurs, however, when left ventricular mass is adjusted by height. This difference is shown in Figure 1A, where the age-adjusted prevalence of left ventricular hypertrophy is plotted against body

Table 1. Prevalence of Underlying Conditions According to Age and Sex

	Age					
	< 30	30-39	40-49	50-59	60-69	70+
Men, *n* (total = 2229)	133	460	549	465	432	190
Hypertension*	9.0	17.0	25.1	36.8	49.2	55.8
Myocardial infarction	0	0.2	1.8	6.7	10.2	15.3
Angina†	0	0.2	0.7	3.2	6.3	10.0
Valvular heart disease	0	2.8	2.7	3.0	8.1	22.6
Women, *n* (total = 2747)	132	585	593	487	582	368
Hypertension*	0.8	2.7	12.7	26.7	43.0	61.7
Myocardial infarction	0	0	0.3	0.6	3.1	5.4
Angina†	0	0.5	0.2	3.7	6.9	12.5
Valvular heart disease	2.3	3.8	3.7	3.7	7.2	16.3

* Blood pressure 140/90 mm Hg or greater, or taking antihypertensive medication.
† Angina pectoris in the absence of history of myocardial infarction.

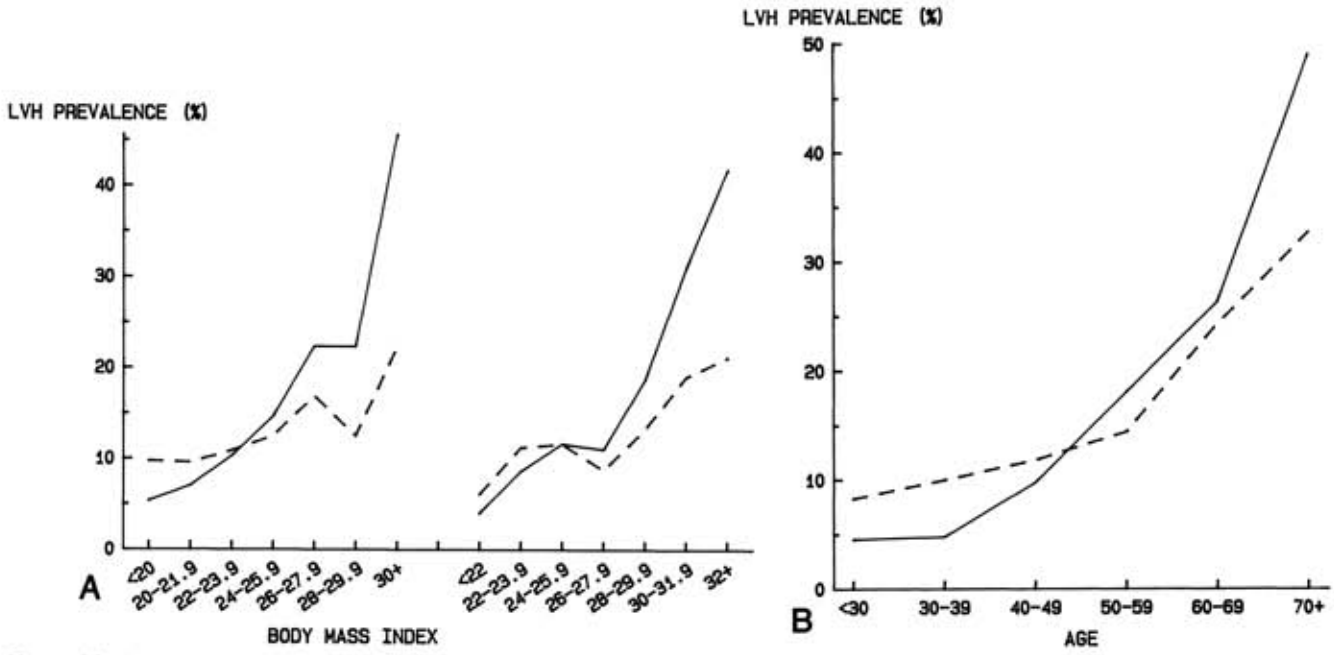

Figure 1A. Age-adjusted prevalence (rate/100) of left ventricular hypertrophy (*LVH*) according to body mass index (kg/m^2). Rates are plotted according to left ventricular mass/height (*solid lines*) and left ventricular mass/body surface area (*dashed lines*) criteria for left ventricular hypertrophy. Trend toward increasing prevalence of left ventricular hypertrophy with increasing body mass index is significant for both criteria tested and in both sexes (women, *left curves;* men, *right curves*) ($P < 0.001$). **Figure 1B.** Prevalence (rate/100) of left ventricular hypertrophy (*LVH*) according to age. Left ventricular mass/height criteria are used. Trend toward increasing prevalence of left ventricular hypertrophy with increasing age is significant in both sexes ($P < 0.001$). Women are shown by a solid line; men by a dashed line.

mass index (a measure of obesity). The association of left ventricular hypertrophy with advancing degrees of obesity becomes attenuated when left ventricular mass/body surface area criteria are used, compared to left ventricular mass/height criteria ($P < 0.001$). For these reasons, Figures 1B, 2, 3, and 4 use left ventricular hypertrophy criteria based on left ventricular mass adjusted for height.

PREVALENCE OF LEFT VENTRICULAR HYPERTROPHY

Left ventricular mass/height criteria for left ventricular hypertrophy were fulfilled in 356 men and 513 women, yielding prevalence rates of 16% and 19% respectively. When left ventricular mass/body surface area criteria were applied, 275 men (12%) and 383 women (14%) were found to have left ventricular hypertropy.

INFLUENCE OF AGE

Prevalence rates of left ventricular hypertrophy are plotted by age and sex in Figure 1B. Left ventricular hypertrophy was found in 6% of participants under age 30 and in 43% of those 70 years of age or older. In the youngest age groups, left ventricular hypertrophy is commoner in men, whereas in older subjects a female predominance occurs. The prevalence of left ventricular hypertrophy increases tenfold from women under age 30 to those 70 years of age or older (4.6% to 48.9%, $P < 0.001$ for trend). Figures 1B, 2, and 3 show a powerful association of left ventricular hypertrophy with advancing age. Multivariate analyses (Table 2) suggest that this association persists independently of the confounding influences of blood pressure, obesity, and coronary and valvular heart disease. The independent association of age with left ventricular hypertrophy is significant in both sexes, with a 15% increase in risk in men, and a 67% increase in women, for each 10-year increment of age.

Table 2. Odds Ratios for Prevalence of Left Ventricular Hypertrophy*

Variable (Increment)	Men		Women	
	Odds Ratio	*P* Value	Odds Ratio	*P* Value
Age (10 years)	1.15	0.017	1.67	<0.001
Systolic blood pressure (20 mm Hg)	1.43	<0.001	1.25	<0.001
Antihypertensive treatment (yes/no)†	1.47	0.014	1.50	0.002
Body mass index (2 kg/m^2)	1.47	<0.001	1.51	<0.001
Myocardial infarction (yes/no)	3.45	<0.001	3.52	0.001
Angina (yes/no)‡	2.01	0.020	. . .	Not significant
Valvular heart disease (yes/no)	3.42	<0.001	2.35	0.001

* Results of multiple logistics regression analysis. Dependent variable is left ventricular hypertrophy (using left ventricular hypertrophy/height criteria). Odds ratios are computed from multiple logistic regression coefficients.
† Currently taking antihypertensive medication.
‡ Angina pectoris in the absence of history of myocardial infarction.

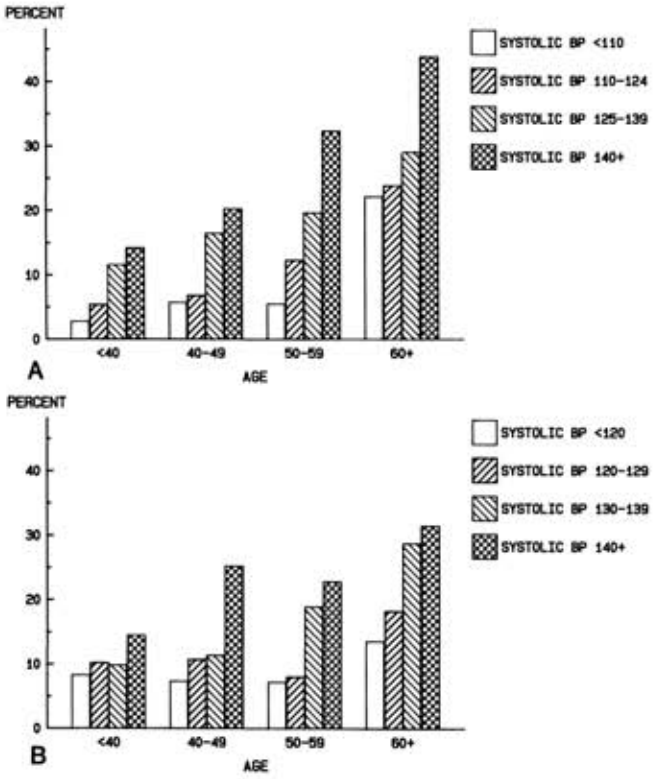

Figure 2A. Age-specific prevalence (rate/100) of left ventricular hypertrophy according to approximate quartiles of systolic blood pressure in women. Left ventricular mass/height criteria are used. Blood pressure (*BP*) measured in mm Hg. **Figure 2B.** Age-specific prevalence of left ventricular hypertrophy according to approximate quartiles of systolic blood pressure in men.

INFLUENCE OF BLOOD PRESSURE

Age-specific rates of left ventricular hypertrophy are plotted according to approximate quartiles of systolic blood pressure and age at the index examination in Figure 2. There is a continuous association of systolic blood pressure with left ventricular hypertrophy. This interaction suggests a dose-response relationship that occurs at levels of systolic blood pressure less than 140 mm Hg, commonly regarded as within the limits of normal (age adjusted, $P < 0.001$, both sexes). In the multivariate analyses (Table 2), systolic blood pressure is independently predictive of left ventricular hypertrophy in both sexes, with a 43% increase in risk for left ventricular hypertrophy in men and a 25% increase in women for a 20 mm Hg increment in systolic blood pressure.

INFLUENCE OF OBESITY

The association of obesity with left ventricular hypertrophy is evident in Figure 1A where age-adjusted rates of left ventricular hypertrophy are plotted against body mass index. In addition, Figure 3 shows the age-specific prevalence of left ventricular hypertrophy, according to approximate quartiles of body mass index. These two approaches indicate that obesity is strongly associated with an increased prevalence of left ventricular hypertrophy. As with blood pressure, there appears to be a dose-response relationship between the severity and duration (as reflected by age) of obesity and the prevalence of left ventricular hypertrophy. Furthermore, an additive interaction between obesity and blood pressure is suggested by Figure 4 in which age-adjusted rates of left ventricular hypertrophy are plotted according to quartiles of body mass index and systolic blood pressure. In both sexes, left ventricular hypertrophy has a 17-fold increase from the group with the lowest pressure and lowest body mass index to the group with highest pressure and highest body mass index. As with age and systolic blood pressure, obesity is independently predictive of left ventricular hypertrophy risk in both sexes, with a 47% increase in men and a 51% increase in women for every 2 kg/m^2 increment in body mass index.

MULTIVARIATE ANALYSIS

In addition to age, systolic blood pressure, and body mass index, which are discussed above, antihypertensive drug therapy, myocardial infarction, and valvular heart disease are independently predictive of left ventricular hypertrophy risk in both sexes (Table 2). In men, angina pectoris in the absence of myocardial infarction is also an independent predictor of left ventricular hypertrophy (odds ratio, 2.01; $P = 0.02$). The multivariate odds ratio for left ventricular hypertrophy in association with myocardial infarction is 3.45 in men ($P < 0.001$) and 3.52 in women ($P = 0.0006$). The odds ratios for left ventricular hypertrophy in persons with valve disease are 3.42 in men ($P < 0.001$) and 2.35 in women ($P < 0.001$). Persons

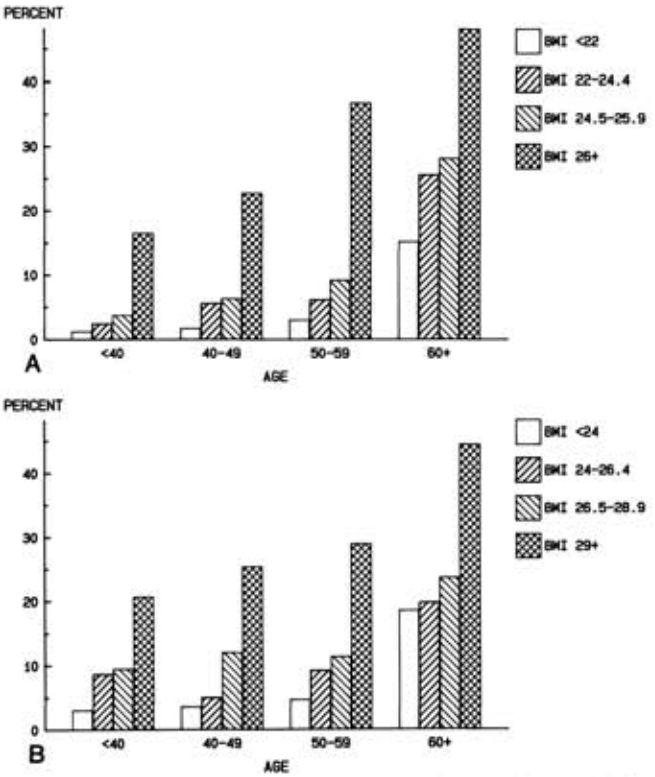

Figure 3A. Age-specific prevalence (rate/100) of left ventricular hypertrophy according to approximate quartiles of body mass index in women. Left ventricular mass/height criteria are used. Body mass index (*BMI*) measured in kg/m^2. **Figure 3B.** Age-specific prevalence of left ventricular hypertrophy according to approximate quartiles of body mass index in men.

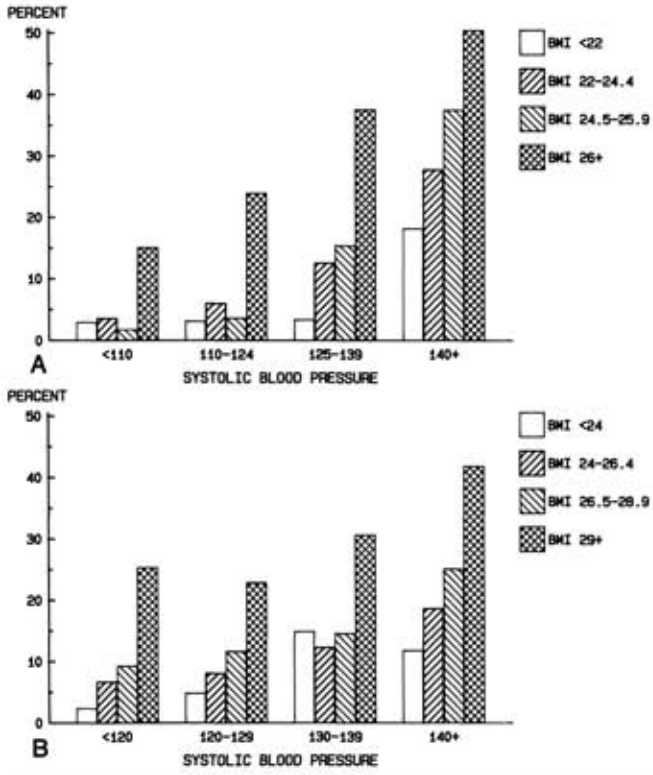

Figure 4A. Age-adjusted prevalence of left ventricular hypertrophy (rate/100) according to approximate quartiles of systolic blood pressure and body mass index in women. Left ventricular mass/height criteria are used. Body mass index (*BMI*) measured in kg/m^2; blood pressure (*BP*) measured in mm Hg. **Figure 4B.** Age-adjusted prevalence of left ventricular hypertrophy according to approximate quartiles of systolic blood pressure and body mass index in men.

taking antihypertensive medications are at 50% increased risk for left ventricular hypertrophy.

Discussion

Although the clinical significance of electrocardiographic left ventricular hypertrophy has been recognized in this study population (1-4), only recently have preliminary data emerged that implicate echocardiographically determined left ventricular hypertrophy as a powerful predictor of cardiovascular morbidity (15) and mortality (16). Although noninvasive methods for estimating left ventricular mass have been available for 15 years (5), criteria for left ventricular hypertrophy based on the distribution of left ventricular mass in a healthy reference population have only recently been developed.

The present study examines the prevalence and potential determinants of this common and often unsuspected condition. Unlike previous reports of the prevalence of echocardiographic left ventricular hypertrophy in selected groups (12-14), the Framingham Heart Study offers an opportunity to define the prevalence of echocardiographic left ventricular hypertrophy in the general population.

In contrast to electrocardiographic left ventricular hypertrophy, which occurs in only 3.2% of the general population (2), echocardiographic left ventricular hypertrophy is a common finding, occurring in 16% to 19% of this study population. These rates are likely to underestimate the prevalence of this condition in the general population due to the selection bias inherent in echocardiography because it is technically difficult to obtain adequate studies in elderly or obese persons, who are at particularly high risk for left ventricular hypertrophy.

As is true of the risk of coronary disease, the prevalence of echocardiographic left ventricular hypertrophy increases dramatically with advancing age (Figure 1B) from 6% in persons less than 30 years of age to 43% in those over age 69. In elderly women the prevalence of left ventricular hypertrophy approaches 50%. Multivariate analysis (Table 2) supports an independent role of age in the development of left ventricular hypertrophy, but this role was more pronounced in women than in men. For every 10-year increment of age, the risk for left ventricular hypertrophy increases 15% in men and 67% in women. The extent to which increasing left ventricular mass is a natural consequence of the aging process, or rather, a reflection of underlying conditions that become more prevalent with advancing age and which predispose to left ventricular hypertrophy (Table 1), deserves additional investigation.

An etiologic role of hypertension in the evolution of electrocardiographic left ventricular hypertrophy has been established in previous Framingham Heart Study reports (2, 3); its association with echocardiographic left ventricular hypertrophy has also been reported (13). The present study confirms and extends previous concepts by showing a seemingly constant and graded effect of systolic blood pressure levels, which are within the limits of normal, on increasing prevalence of left ventricular hypertrophy (Figure 2). These data suggest a dose-response relationship between blood pressure and left ventricular hypertrophy, supporting the hypothesis that both the duration and the severity of hypertension contribute to the occurrence of this condition. Additional longitudinal observation would be required to confirm this. The multivariate analysis suggests a significant independent role of blood pressure in promoting left ventricular hypertrophy, with a 43% increase in prevalence in men and a 25% increase in women, for every 20 mm Hg increase in systolic blood pressure. Furthermore, antihypertensive drug therapy is independently predictive of left ventricular hypertrophy, suggesting that even after controlling for the level of blood pressure, medically treated hypertensive patients are more likely to have cardiac end-organ sequelae of their hypertension. This finding may reflect the likelihood that drug therapy was initiated preferentially in the more severely affected hypertensive subjects.

Similarly, the present study extends the current understanding of the cardiac structural consequences of obesity (25-27) by showing a graded effect of obesity, as measured by body mass index, upon prevalence of left ventricular hypertrophy (Figures 1A, 3 and 4). Across the range of observed body mass index values, there is a tenfold increase in prevalence of left ventricular hypertrophy in men, and a ninefold increase in women (Figure 3). Similar, but less striking, results are obtained when age-

adjusted prevalence of left ventricular hypertrophy is plotted against subscapular skinfold thickness (a measure of adiposity). Obesity is also a powerful independent predictor of left ventricular hypertrophy in the multivariate model (odds ratio per 2 kg/m^2 increment of body mass index, 1.47 in men, 1.51 in women).

Some investigators (28, 29) have suggested that hypertension in the setting of obesity has a better prognosis than when it occurs in lean persons. Assuming that echocardiographic left ventricular hypertrophy carries a poor prognosis (15, 16), the present study does not support this hypothesis. To the contrary, this study strongly indicates that obesity and hypertension have independent and additive roles in the pathogenesis of cardiac hypertrophy. There is no suggestion of attenuation of the cardiac changes of hypertension in obese persons. At each level of blood pressure studied, and in both sexes, increasing degrees of obesity are associated with increased prevalence of left ventricular hypertrophy (Figure 4).

Other conditions that may predispose a person to left ventricular hypertrophy are coronary disease and valvular heart disease. Coronary disease, particularly after myocardial infarction, can promote left ventricular dilation. Valvular heart disease can promote left ventricular hypertrophy by virtue of increased pressure or volume work on the heart. The multivariate analysis (Table 2) is consistent with the independent roles of these conditions in the pathogenesis of left ventricular hypertrophy. A history of myocardial infarction confers more than a threefold increase in risk for left ventricular hypertrophy in both sexes, whereas angina pectoris, in the absence of myocardial infarction, is associated with a doubling of risk in men. Valvular heart disease is also independently associated with prevalence of left ventricular hypertrophy (odds ratio, 3.42 in men, 2.35 in women).

Additionally, this study offers an opportunity to better define optimal echocardiographic criteria for left ventricular hypertrophy. The use of criteria that do not adjust left ventricular mass for body size results in an undesirable increase in the prevalence of left ventricular hypertrophy in taller persons ($P < 0.001$). It is customary to correct left ventricular mass by body surface area (which takes into account both weight and height). When left ventricular mass/body surface area criteria for left ventricular hypertrophy are applied, the relationship of obesity to left ventricular hypertrophy becomes attenuated (Figure 1B). This "forgiveness" of obesity does not occur when left ventricular mass/height criteria are used, because this method makes no allowance for adiposity. For these reasons, and because there is a strong body of evidence that obesity predisposes to pathologic alteration in cardiac structure (25-27), the use of left ventricular mass/height criteria for left ventricular hypertrophy are encouraged.

The present study supports hypertension control and weight reduction as two approaches likely to minimize development of left ventricular hypertrophy or, possibly, to promote its regression (28, 29). Numerous studies (30-33) have shown left ventricular hypertrophy regression in response to antihypertensive drug therapy. Recently, greater attention has been paid to the importance of weight loss in promoting left ventricular hypertrophy regression (34). The prognostic significance of left ventricular hypertrophy regression requires additional evaluation.

Ideally, outcome-guided left ventricular hypertrophy criteria are best suited for clinical application, but such criteria are not yet available. The present study offers a rationale for the use of sex-specific, height-adjusted criteria for left ventricular hypertrophy based on the distribution of left ventricular mass in a healthy reference population. Although data to support the height correction of left ventricular mass are provided, such evidence at present is only circumstantial. Additional follow-up of this population for cardiovascular disease sequelae will ultimately determine the best strategy for the echocardiographic determination of left ventricular hypertrophy. The independent prognostic significance of echocardiographically determined left ventricular hypertrophy will require extensive follow-up of persons with this common finding.

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