

The New England Journal of Medicine

© Copyright, 1999, by the Massachusetts Medical Society

VOLUME 340

APRIL 22, 1999

NUMBER 16



TRENDS IN THE PREVALENCE OF HYPERTENSION, ANTIHYPERTENSIVE THERAPY, AND LEFT VENTRICULAR HYPERTROPHY FROM 1950 TO 1989

AREND MOSTERD, M.D., PH.D., RALPH B. D'AGOSTINO, PH.D., HALIT SILBERSHATZ, PH.D., PAMELA A. SYTKOWSKI, PH.D., WILLIAM B. KANNEL, M.D., M.P.H., DIEDERICK E. GROBBEE, M.D., PH.D., AND DANIEL LEVY, M.D.

ABSTRACT

Background Men and women with hypertension are at increased risk for cardiovascular disease, especially when left ventricular hypertrophy is present. We examined temporal trends in the use of antihypertensive medications and studied the relation between their use, the prevalence of high blood pressure, and the presence of electrocardiographic evidence of left ventricular hypertrophy.

Methods A total of 10,333 participants in the Framingham Heart Study who were 45 to 74 years of age underwent a total of 51,756 examinations from 1950 to 1989. Data were obtained on blood pressure and the use of antihypertensive medications, and electrocardiograms were assessed for left ventricular hypertrophy. The generalized-estimating-equation method was used to test for trends over time.

Results From 1950 to 1989, the rate of use of antihypertensive medications increased from 2.3 percent to 24.6 percent among men and from 5.7 percent to 27.7 percent among women. The age-adjusted prevalence of systolic blood pressure of at least 160 mm Hg or diastolic blood pressure of at least 100 mm Hg declined from 18.5 percent to 9.2 percent among men and from 28.0 percent to 7.7 percent among women. This decline was accompanied by age-adjusted reductions in the prevalence of electrocardiographic evidence of left ventricular hypertrophy, from 4.5 percent to 2.5 percent among men and from 3.6 percent to 1.1 percent among women.

Conclusions Our findings support the notion that the increasing use of antihypertensive medication has resulted in a reduced prevalence of high blood pressure and a concomitant decline in left ventricular hypertrophy in the general population. Our observations may in part explain the considerable decline in mortality from cardiovascular disease observed since the late 1960s. (N Engl J Med 1999;340:1221-7.)

©1999, Massachusetts Medical Society.

HYPERTENSION is an important contributor to morbidity and mortality from cardiovascular disease.^{1,3} The proportion of persons with hypertension who are receiving treatment has risen steadily over the past four decades.^{2,4} Consequently, the number of people with elevated systolic or diastolic blood pressure has declined in the United States.⁴ Multiple clinical trials have shown that treatment of hypertension reduces the incidence of associated cardiovascular disorders.^{2,5} Long-term benefits of antihypertensive therapy have been demonstrated for the general population as well.⁶ However, the contribution of improved treatment of hypertension to the decline in mortality from ischemic heart disease is difficult to assess in the population at large.⁷⁻¹⁰

The risk of cardiovascular disease at any level of high blood pressure increases markedly for patients with damage to the heart, kidneys, brain, or large arteries.² Left ventricular hypertrophy is causally related to high blood pressure and represents hypertensive target-organ damage.^{2,11,12} Persons with left ventricular hypertrophy are at increased risk for a variety of cardiovascular sequelae, including angina pectoris, myocardial infarction, stroke, heart failure, and sudden death.¹³⁻¹⁶ Treatment of high blood pressure has been shown to prevent the development of left ventricular hypertrophy or to reverse it.^{12,13,17-19} Electro-

From the National Heart, Lung, and Blood Institute's Framingham Heart Study, Framingham, Mass. (A.M., R.B.D., H.S., P.A.S., W.B.K., D.L.); the Thoraxcenter and Division of Cardiology (A.M.) and Department of Epidemiology and Biostatistics (A.M., D.E.G.), Erasmus University Medical School, Rotterdam, the Netherlands; the Julius Center for Patient-Oriented Research, Utrecht University, Utrecht, the Netherlands (D.E.G.); the National Heart, Lung, and Blood Institute, Bethesda, Md. (D.L.); the Divisions of Cardiology and Epidemiology, Beth Israel Deaconess Medical Center, Boston (D.L.); and the Department of Mathematics (R.B.D., H.S.) and the Division of Epidemiology and Preventive Medicine (W.B.K., D.L.), Boston University School of Medicine, Boston. Address reprint requests to Dr. Levy at the Framingham Heart Study, 5 Thurber St., Framingham, MA 01702.

cardiographic evidence of reversal of left ventricular hypertrophy is associated with a decreased risk of cardiovascular disease.¹⁴

The Framingham Heart Study has obtained blood-pressure measurements, information on the use of antihypertensive medications, and electrocardiograms in a standardized manner since its inception in 1948. The goals of the present investigation were to describe temporal trends in the frequency of high blood pressure and its treatment in a sample of the general population and to determine whether better control of high blood pressure has resulted in a concomitant decline in the prevalence of hypertensive target-organ damage, as evidenced by electrocardiographic left ventricular hypertrophy.

METHODS

Study Population and Cardiovascular Examination

The Framingham Heart Study began in 1948 with the enrollment of 5209 men and women, free of cardiovascular disease, who were 28 to 62 years of age.²⁰ These participants have since been examined every two years. In 1971 another cohort of 5124 men and women who were the children or the spouses of the children of the original participants was enrolled (the Offspring Study).²¹ Because left ventricular hypertrophy is rare in the young and no subjects were more than 75 years of age in the early years of the study, the present analysis has been restricted to persons who were 45 to 74 years old during the period from 1950 to 1989.

Each examination included the taking of an extensive cardiovascular history, a physical examination, blood-pressure determinations, 12-lead electrocardiography, and measurement of other physiologic variables. Morbidity and mortality were continuously monitored by hospital surveillance and by communication with the personal physicians and relatives of study participants. All new cardiovascular events were reviewed by a panel of three experienced investigators. Detailed descriptions of the sampling methods, examination techniques and procedures, and criteria for various end points related to cardiovascular disease have been published.^{20,21}

Definition and Categorization of Normal and High Blood Pressure

Recorded systolic and diastolic blood pressure was the average of two separate measurements made by the physician at each examination. High-blood-pressure stages, irrespective of treatment, were defined according to the criteria established by the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure, as follows: stage 1, systolic blood pressure of 140 to 159 mm Hg or diastolic blood pressure of 90 to 99 mm Hg; stage 2, systolic blood pressure of 160 to 179 mm Hg or diastolic blood pressure of 100 to 109 mm Hg; stage 3, systolic blood pressure of 180 to 209 mm Hg or diastolic blood pressure of 110 to 119 mm Hg; and stage 4, systolic blood pressure of at least 210 mm Hg or diastolic blood pressure of at least 120 mm Hg.^{2,3} The sixth revision of the criteria eliminated stage 4 by combining it with stage 3. However, stage 4 is reported here because it was available throughout this investigation.

Electrocardiographic Methods and Definition of Left Ventricular Hypertrophy

Resting 12-lead electrocardiograms were routinely obtained at each clinic visit. All electrocardiograms obtained from the 1st to the 20th examination of the original cohort and from the 1st to the 4th examination of the participants in the Offspring Study were used to determine the prevalence of left ventricular hypertrophy. The initial diagnosis was made by the examining physician at the time of the routine clinic visit if at least one of the following voltage cri-

teria was met: R wave >1.1 mV in aVL; R wave \geq 2.5 mV in V₅ or V₆; S wave \geq 2.5 mV in V₁ or V₂; sum of S wave in V₁ or V₂ plus R wave in V₅ or V₆ \geq 3.5 mV; and sum of R wave in I and S wave in III \geq 2.5 mV. One reader, blinded to clinical information, validated the presence of left ventricular hypertrophy for all electrocardiograms identified by the examining physician as showing left ventricular hypertrophy. In addition, the amplitudes of the R wave in aVL and the S wave in V₃ were measured; their sum was considered an index of the severity of left ventricular hypertrophy.^{22,23}

All electrocardiographic voltages were measured to the nearest 0.1 mV. All subsequent electrocardiograms of subjects in whom left ventricular hypertrophy had been diagnosed by the examining physician were reviewed as well. All tracings were then analyzed by a second blinded reader who reviewed voltage criteria and measurements and graded the repolarization features. Repolarization was categorized as normal, mildly abnormal (ST-T flattening, isolated ST depression, or T-wave inversion), or severely abnormal ("strain" pattern: ST depression in association with inverted or biphasic T waves).

For the present analyses, a strict definition of left ventricular hypertrophy was used. Electrocardiograms were eligible for inclusion only if a diagnosis of left ventricular hypertrophy was confirmed on blinded review. In addition, the sum of the R wave in aVL and the S wave in V₃ had to be greater than 1.3 mV, and repolarization had to be either mildly or severely abnormal. A combined voltage of 1.3 mV represented the 25th percentile of a reference group of persons with left ventricular hypertrophy in a previous study.¹⁴ The 50th and 75th percentiles in that study were 1.8 and 2.3 mV, respectively. Electrocardiograms indicating complete right or left bundle-branch block, Wolff-Parkinson-White syndrome, or prior Q-wave myocardial infarction, and all tracings obtained in subjects who were receiving digoxin, were excluded from this analysis.

Statistical Analysis

The age-adjusted mean values for blood pressure and body-mass index, rate of use of antihypertensive medications, and prevalence of hypertension of stage 2 or higher, irrespective of treatment, as well as the prevalence of left ventricular hypertrophy were determined for men and women separately for the four decades under study (1950 through 1959, 1960 through 1969, 1970 through 1979, and 1980 through 1989). Age adjustment was performed by a least-squares regression approach. The generalized-estimating-equation method was used to test for trends in use of antihypertensive medications, the prevalence of hypertension of stage 2 or higher, and the prevalence of left ventricular hypertrophy.²⁴ This method adjusts for repeated measurements in the same persons. The model included age and year of examination as independent variables. The year of examination was used to test for temporal trends in prevalence. The generalized estimating equation was also used to determine whether the trends in prevalence persisted when adjustments were made for age and body-mass index. All statistical tests were two-sided. With the generalized-estimating-equation approach, we used the robust estimate of the standard errors. A result was considered statistically significant if the P value was less than 0.05.

Pooled logistic analysis was used to relate age, systolic blood pressure, body-mass index, use of antihypertensive medications, and decade of examination (the independent variables) to the presence or absence of left ventricular hypertrophy (the dependent variable).²⁵

RESULTS

Study Population

Left ventricular hypertrophy developed in 1829 of the 5209 original subjects of the Framingham Heart Study during follow-up through 1989. Among the 5124 participants in the Offspring Study, whose enrollment started in 1971, left ventricular hypertrophy

developed in 152. After exclusions, a total of 1265 participants, 45 to 74 years old, had left ventricular hypertrophy between 1950 and 1989 (Table 1). Our analyses are based on a total of 51,756 examinations.

Antihypertensive Treatment, Blood Pressure, and Electrocardiographic Left Ventricular Hypertrophy

Table 2 presents age-adjusted temporal trends in blood pressure, body-mass index, use of antihypertensive medications, and prevalence of high blood pressure. The use of antihypertensive medications in-

creased from 2.3 percent among men and 5.7 percent among women in the 1950s to 24.6 percent among men and 27.7 percent among women in the 1980s.

The general decline in the prevalence of high blood pressure (Table 2) was accompanied by a greater proportional decline in the prevalence of the higher stages of blood pressure (Table 3). The mean decline in the prevalence of stage 4 hypertension was more than 60 percent per decade among both men and women, as compared with a 29 percent decline in the prevalence of hypertension of stage 2 or higher

TABLE 1. STUDY POPULATION.

VARIABLE	ORIGINAL COHORT		OFFSPRING COHORT		TOTAL
	MEN	WOMEN	MEN	WOMEN	
Subjects					
Subjects at examination 1	2,336	2,873	2483	2641	10,333
Subjects with left ventricular hypertrophy*	839	990	125	27	1,981
Subjects 45–74 yr old from 1950 to 1989					
No. of examinations undergone	21,099	27,979	3691	3756	56,525
Subjects with left ventricular hypertrophy	695	702	81	20	1,498
Electrocardiographic exclusions					
Prior Q-wave myocardial infarction	25	10	1	0	36
Bundle-branch block	19	22	3	1	45
Wolff–Parkinson–White syndrome	0	0	0	0	0
Use of digoxin	56	96	0	0	152
Remaining subjects with left ventricular hypertrophy	595	574	77	19	1,265
Sample for electrocardiographic analysis					
No. of examinations undergone (after application of electrocardiographic exclusion criteria to all participants)	18,311	26,286	3499	3660	51,756

*These subjects had electrocardiograms with a combined voltage (the sum of the R wave in lead aVL and the S wave in lead V₃) that was greater than 1.3 mV and repolarization abnormalities, in addition to fulfilling standard voltage criteria (see the Methods section).

TABLE 2. AGE-ADJUSTED TEMPORAL TRENDS IN BLOOD PRESSURE, USE OF ANTIHYPERTENSIVE MEDICATIONS, AND PREVALENCE OF HIGH BLOOD PRESSURE AMONG MEN AND WOMEN 45 TO 74 YEARS OF AGE.

VARIABLE	MEN					WOMEN				
	1950s	1960s	1970s	1980s	MEAN CHANGE PER DECADE*	1950s	1960s	1970s	1980s	MEAN CHANGE PER DECADE*
No. of examinations	5695	6882	4766	4467		7552	9753	6828	5813	
Mean age (yr)	54	57	61	59		54	58	62	61	
Mean blood pressure (mm Hg)										
Systolic	137.4	137.3	134.7	133.2	-1.6 (-2.3)	145.3	139.9	132.6	130.4	-4.7 (-4.6)
Diastolic	84.5	83.7	82.5	81.8	-1.0 (-1.5)	85.7	82.7	79.2	77.8	-2.5 (-2.5)
Mean body-mass index†	25.9	26.2	26.6	27.2	+0.5	26.3	25.7	25.5	25.8	-0.03
Use of antihypertensive medications (%)	2.3	7.3	16.3	24.6	+128 (+123)	5.7	13.8	20.6	27.7	+70 (+78)
Stage 2 or higher hypertension (%‡)	18.5	17.5	14.2	9.2	-25 (-29)	28.0	21.2	11.0	7.7	-42 (-43)

*Age-adjusted values are given, followed in parentheses by the values adjusted for age and body-mass index. All changes were significant (P<0.001), with the exception of body-mass index in women (P=0.77).

†The body-mass index is the weight in kilograms divided by the square of the height in meters.

‡Subjects had a systolic blood pressure of at least 160 mm Hg or a diastolic blood pressure of at least 100 mm Hg, irrespective of the use or nonuse of antihypertensive medications.

TABLE 3. AGE-ADJUSTED TEMPORAL TRENDS IN THE SEVERITY OF HIGH BLOOD PRESSURE IRRESPECTIVE OF TREATMENT AMONG MEN AND WOMEN 45 TO 74 YEARS OF AGE.

VARIABLE	MEN					WOMEN				
	1950s	1960s	1970s	1980s	MEAN CHANGE PER DECADE*	1950s	1960s	1970s	1980s	MEAN CHANGE PER DECADE*
No. of examinations	5695	6882	4766	4467		7552	9753	6828	5813	
Hypertension (%)†										
Stage 2 or higher	18.5	17.5	14.2	9.2	-25 (-29)	28.0	21.2	11.0	7.7	-42 (-43)
Stage 3 or higher	6.7	5.3	2.7	1.7	-39 (-42)	11.0	7.7	2.2	0.9	-55 (-54)
Stage 4	1.8	0.8	0.3	0.1	-59 (-63)	2.7	1.4	0.1	0.1	-69 (-68)

*Age-adjusted values are given, followed in parentheses by the values adjusted for age and body-mass index. All changes are significant (P<0.001).

†Hypertension stages were defined as follows: stage 2, ≥160/100 mm Hg; stage 3, ≥180/110 mm Hg; and stage 4, ≥210/120 mm Hg.^{2,3}

TABLE 4. AGE-ADJUSTED TEMPORAL TRENDS IN PREVALENCE AND SEVERITY OF ELECTROCARDIOGRAPHICALLY CONFIRMED LEFT VENTRICULAR HYPERTROPHY AMONG MEN AND WOMEN 45 TO 74 YEARS OF AGE.

VARIABLE*	MEN					MEAN CHANGE PER DECADE†	P VALUE‡	WOMEN					MEAN CHANGE PER DECADE†	P VALUE‡
	1950s	1960s	1970s	1980s	1950s			1960s	1970s	1980s				
No. of examinations	5695	6882	4766	4467				7552	9753	6828	5813			
LVH (no.)	222	217	110	123				208	202	88	95			
LVH (%)	4.5	3.2	1.8	2.5	-24 (-23)	<0.01		3.6	2.2	0.6	1.1	-41 (-41)	<0.01	
Mean voltage§	2.49	2.34	2.19	2.21	-0.07 (-0.08)	0.03		2.45	2.29	2.22	2.26	-0.06 (-0.06)	0.06	
Voltage criteria (%)¶														
LVH ₂₅	0.7	0.6	0.5	0.5	-16 (-16)	0.14		0.7	0.5	0.1	0.3	-37 (-39)	<0.01	
LVH ₅₀	1.4	0.9	0.6	1.0	-14 (-16)	0.14		1.0	0.6	0.2	0.3	-38 (-38)	<0.01	
LVH ₇₅	2.4	1.7	0.8	1.0	-36 (-37)	<0.01		1.9	1.1	0.3	0.4	-47 (-46)	<0.01	
Repolarization (%)														
Mildly abnormal	2.9	2.3	1.2	1.6	-19 (-20)	<0.01		2.2	1.4	0.3	0.7	-35 (-35)	<0.01	
Severely abnormal	1.6	0.9	0.6	0.8	-22 (-23)	0.07		1.4	0.9	0.3	0.4	-37 (-37)	<0.01	

*LVH denotes left ventricular hypertrophy.

†Age-adjusted values are given, followed in parentheses by the values adjusted for age and body-mass index.

‡P values are for age-adjusted changes. P values were similar for changes adjusted for age and body-mass index.

§The mean voltage is the sum of the R wave in lead aVL and the S wave in lead V₃.

¶The voltage criteria were as follows: LVH₂₅, mean voltage >1.3 mV and ≤1.8 mV; LVH₅₀, mean voltage >1.8 mV and ≤2.3 mV; and LVH₇₅, mean voltage >2.3 mV (see the Methods section).

||Mildly abnormal repolarization is defined by ST-T flattening, isolated ST depression, or T-wave inversion. Severely abnormal repolarization is defined by a "strain" pattern: ST depression in association with inverted or biphasic T waves.

among men and a 43 percent decline among women. The prevalence of left ventricular hypertrophy showed concomitant declines (Table 4). Among men with left ventricular hypertrophy, the mean combined voltage of the R wave in lead aVL plus the S wave in lead V₃, an index of the severity of hypertrophy, declined from 2.49 mV in the 1950s to 2.21 mV in the 1980s. Among women these figures were 2.45 and 2.26 mV, respectively. There was a greater decline in the prevalence of severe left ventricular hypertrophy (37 percent per decade among men and 46 percent per decade among women) than in the prevalence of milder degrees of hypertrophy.

As expected, left ventricular hypertrophy was

strongly associated with age (Table 5). Multivariate odds ratios for the presence of left ventricular hypertrophy in relation to predictor variables revealed an important role of systolic blood pressure. A higher body-mass index was associated with a higher prevalence of left ventricular hypertrophy among men and a lower prevalence among women. Subjects treated with antihypertensive medications were more likely than others to have left ventricular hypertrophy, reflecting the tendency to initiate drug treatment in hypertensive patients with target-organ damage. As compared with the 1950s, left ventricular hypertrophy was progressively less common in the 1960s, 1970s, and 1980s.

TABLE 5. MULTIVARIATE ODDS RATIOS FOR THE PRESENCE OF ELECTROCARDIOGRAPHICALLY CONFIRMED LEFT VENTRICULAR HYPERTROPHY ACCORDING TO VARIOUS RISK FACTORS.*

RISK FACTOR	MEN		WOMEN	
	ODDS RATIO (95% CI)	P VALUE	ODDS RATIO (95% CI)	P VALUE
Age (per 10 yr)	1.36 (1.19–1.56)	<0.001	2.03 (1.77–2.33)	<0.001
Systolic blood pressure (per 20 mm Hg)	2.26 (2.09–2.44)	<0.001	1.90 (1.76–2.06)	<0.001
Body-mass index (per 2 units)	1.06 (1.01–1.11)	0.015	0.91 (0.87–0.95)	<0.001
Use of antihypertensive medications (yes vs. no)	1.86 (1.48–2.35)	<0.001	2.86 (2.33–3.51)	<0.001
Decade†				
1950s	1.00		1.00	
1960s	0.63 (0.51–0.78)	<0.001	0.41 (0.32–0.52)	<0.001
1970s	0.44 (0.33–0.58)	<0.001	0.23 (0.17–0.31)	<0.001
1980s	0.40 (0.27–0.58)	<0.001	0.29 (0.21–0.42)	<0.001

*CI denotes confidence interval.

†Patients examined during the 1950s made up the reference group.

When age and body-mass index were controlled for in the generalized-estimating-equation analysis, the increased use of antihypertensive medications as well as the declines over time in the prevalence of high blood pressure and electrocardiographic left ventricular hypertrophy remained significant (Tables 2, 3, and 4).

DISCUSSION

We analyzed the relations between the increasing use of antihypertensive medications and concomitant trends in the prevalence of high blood pressure and electrocardiographic evidence of left ventricular hypertrophy in a general population sample followed from 1950 through 1989. Our analyses are consistent with the hypothesis that the introduction and widespread use of antihypertensive medications over the past 40 years have resulted in a decline in the prevalence of high blood pressure. The decline was particularly striking for more severe hypertension (stages 3 and 4). A parallel decrease in the prevalence of cardiac target-organ damage, as indicated by electrocardiographic evidence of left ventricular hypertrophy, was also observed. In addition, among those with left ventricular hypertrophy, the mean voltage (the sum of the R wave in lead aVL and the S wave in lead V₃) also declined. Although only moderate declines in mean blood pressure and mean voltages were observed in our population, the prevalence of left ventricular hypertrophy decreased appreciably, possibly as a result of the near-elimination of the more severe stages of hypertension.

Our finding of decreases in the prevalence of hypertension is in accordance with the findings of the National Health and Nutrition Examination Surveys, indicating that the awareness, treatment, and control of hypertension in the United States have improved over the years.⁴ Interestingly, in our study,

the age-adjusted mean blood-pressure levels (both diastolic and systolic) decreased to a greater degree among women than among men (15 mm Hg systolic and 8 mm Hg diastolic among women and 4 mm Hg systolic and 3 mm Hg diastolic among men). This may be due to the increase in body-mass index that occurred in men, whereas body-mass index declined over time in women. A 10-lb (4.5-kg) increase in weight corresponds to an increase of 4.5 mm Hg in systolic blood pressure.²⁶ Part of the increase in body-mass index among men may be explained by the decreasing numbers of male smokers. Among women the number of smokers increased from the 1950s to the 1980s²⁷ and declined thereafter.²⁸ Data from the National Health and Nutrition Examination Surveys also indicate an increase in obesity from 1960 to 1991 among men of all ages and a decline among women 60 to 74 years of age from 1960 to 1980, with a rise thereafter.²⁹

Left ventricular hypertrophy is an important risk factor for cardiovascular disease.^{12,16} It was found to be the feature on electrocardiography at rest that was associated with the highest risk of fatal coronary heart disease in a group of 7682 men who were followed for 12 years; the relative risk was 11.4.¹⁶ The mechanisms by which left ventricular hypertrophy is associated with the increased risk of cardiovascular sequelae are not fully understood. Hypertrophy increases the myocardial oxygen requirement, which, when supply is decreased because of atherosclerosis and decreased coronary reserve, imposes a risk of ischemia. This is especially true when repolarization abnormalities are present.³⁰ Left ventricular hypertrophy is also associated with an increased risk of arrhythmias^{31,32} and sudden death.^{11,33}

Blood pressure is a major determinant of left ventricular hypertrophy (in terms of both voltage criteria and repolarization abnormalities).^{12,14} Regression of

left ventricular hypertrophy has been observed in hypertensive patients in response to treatment with antihypertensive drugs,^{13,18,19,34,35} and it apparently reduces the risk of cardiovascular disease.^{14,35} Over 43 million Americans have hypertension, of whom only about half are being treated with drugs; only about one quarter have their hypertension adequately controlled.⁴ Since high blood pressure is one of the major risk factors for cardiovascular disease, it is a reasonable assumption that progress in the detection, treatment, and control of hypertension has contributed substantially to national declines in mortality from coronary heart disease and stroke.^{3,6,8,10} According to one estimate, antihypertensive treatment may account for as much as 18 percent of the observed decline in mortality from coronary heart disease between 1968 and 1976.⁷ The declines in both the prevalence and the severity of left ventricular hypertrophy, coinciding with the decline in mean blood pressure and the near-disappearance of stage 4 hypertension in our population-based study, can be interpreted as favorable changes in two major risk factors for cardiovascular disease, which on a national level may have contributed to the declines of more than 50 percent in mortality from cardiovascular disease observed since 1950.³⁶

Because of the observational nature of this study, measures to control hypertension (whether pharmacologic treatment or lifestyle interventions) were not randomly assigned, and there was no control group. Age and weight, the two main determinants of blood pressure apart from pharmacologic treatment,² were controlled for in the analyses. The influence of temporal trends in other risk factors and the possible adoption of healthier lifestyles were not taken into account. It is, however, unlikely that the latter factors accounted for the marked decreases in the prevalence of high blood pressure and its consequences, such as the almost complete disappearance of stage 3 and 4 hypertension. Other than treatment of high blood pressure, aggressive management of other risk factors did not gain widespread acceptance until the 1980s.

This was a longitudinal study of blood-pressure levels, use of antihypertensive medications, and hypertensive target-organ damage in a general population sample of more than 10,000 persons who underwent 51,756 examinations with follow-up. Referral bias was less likely to have occurred in this study than in hospital- or clinic-based studies. The participants were examined at regular intervals, and morbidity and mortality were continuously monitored.

Changing diagnostic techniques and nonrandom attrition, favoring the continued participation of healthier persons,³⁷ may result in a certain degree of bias when temporal trends within cohorts are analyzed. Measurements of weight and blood pressure were performed in a standardized manner that did not change during the study period. Information on

the use of antihypertensive medication was routinely obtained. However, the electrocardiographic coding form filled out by the examining physicians underwent minor changes during the course of the study, and it is conceivable that this affected the coding of hypertrophy. To minimize any potential bias, we reread all electrocardiograms that indicated left ventricular hypertrophy and used a strict definition of left ventricular hypertrophy, excluding mild forms.

This investigation can be perceived as a dynamic population study, with participants entering on reaching 45 and leaving at 75 years of age; moreover, members of the original Framingham Heart Study cohort as well as participants in the Offspring Study were included. These facts should attenuate the possible effects of nonrandom attrition.

Finally, racial differences in the prevalence of hypertension⁴ and in the usefulness of electrocardiographic criteria for the diagnosis of left ventricular hypertrophy³⁸ have been reported; since the Framingham Heart Study sample is predominantly white, the results may not be applicable to other racial groups.

The present analyses cannot prove that the improvement in blood-pressure control caused the decline in the prevalence of left ventricular hypertrophy that we observed. We can, however, conclude that these trends were concurrent and are consistent with a causal relation. The concomitant decline in the severity of left ventricular hypertrophy provides further support for a cause-and-effect relation.

Supported in part by a contract (N01-HC-38038) with the National Heart, Lung, and Blood Institute.

REFERENCES

1. Stamler J, Stamler R, Neaton JD. Blood pressure, systolic and diastolic, and cardiovascular risks: US population data. *Arch Intern Med* 1993;153:598-615.
2. The sixth report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *Arch Intern Med* 1997;157:2413-45. [Erratum, *Arch Intern Med* 1998;158:573.]
3. The fifth report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *Arch Intern Med* 1993;153:154-83.
4. Burt VL, Whelton P, Roccella EJ, et al. Prevalence of hypertension in the US adult population: results from the Third National Health and Nutrition Examination Survey, 1988-1991. *Hypertension* 1995;25:305-13.
5. Collins R, Peto R, MacMahon S, et al. Blood pressure, stroke, and coronary heart disease. 2. Short-term reductions in blood pressure: overview of randomised drug trials in their epidemiological context. *Lancet* 1990;335:827-38.
6. Sytkowski PA, D'Agostino RB, Belanger AJ, Kannel WB. Secular trends in long-term sustained hypertension, long-term treatment, and cardiovascular mortality: the Framingham Heart Study 1950 to 1990. *Circulation* 1996;93:697-703.
7. Goldman L, Cook EF. The decline in ischemic heart disease mortality rates: an analysis of the comparative effects of medical interventions and changes in lifestyle. *Ann Intern Med* 1984;101:825-36.
8. Hunink MG, Goldman L, Tosteson AN, et al. The recent decline in mortality from coronary heart disease, 1980-1990: the effect of secular trends in risk factors and treatment. *JAMA* 1997;277:535-42.
9. Rosamond WD, Chambless LE, Folsom AR, et al. Trends in the incidence of myocardial infarction and in mortality due to coronary heart disease, 1987 to 1994. *N Engl J Med* 1998;339:861-7.
10. Levy D, Thom TJ. Death rates from coronary disease — progress and a puzzling paradox. *N Engl J Med* 1998;339:915-7.

11. Frohlich ED, Apstein C, Chobanian AV, et al. The heart in hypertension. *N Engl J Med* 1992;327:998-1008. [Erratum, *N Engl J Med* 1992; 327:1768.]
12. Chambers J. Left ventricular hypertrophy. *BMJ* 1995;311:273-4.
13. MacMahon S, Collins G, Rautaharju P, et al. Electrocardiographic left ventricular hypertrophy and effects of antihypertensive drug therapy in hypertensive participants in the Multiple Risk Factor Intervention Trial. *Am J Cardiol* 1989;63:202-10.
14. Levy D, Salomon M, D'Agostino RB, Belanger AJ, Kannel WB. Prognostic implications of baseline electrocardiographic features and their serial changes in subjects with left ventricular hypertrophy. *Circulation* 1994;90: 1786-93.
15. Sullivan JM, Vander Zwaag RV, el-Zeky F, Ramanathan KB, Mirvis DM. Left ventricular hypertrophy: effect on survival. *J Am Coll Cardiol* 1993;22:508-13.
16. Knutsen R, Knutsen SF, Curb JD, Reed DM, Kautz JA, Yano K. The predictive value of resting electrocardiograms for 12-year incidence of coronary heart disease in the Honolulu Heart Program. *J Clin Epidemiol* 1988;41:293-302.
17. The Hypertension Detection and Follow-up Program Cooperative Group. Five-year findings of the Hypertension Detection and Follow-up Program: prevention and reversal of left ventricular hypertrophy with anti-hypertensive drug therapy. *Hypertension* 1985;7:105-12.
18. Ashizawa N, Seto S, Kitano K, et al. Effects of blood pressure changes on development and regression of electrocardiographic left ventricular hypertrophy: a 26 year longitudinal study. *J Am Coll Cardiol* 1989;13:165-72.
19. Schmieder RE, Martus P, Klingbeil A. Reversal of left ventricular hypertrophy in essential hypertension: a meta-analysis of randomized double-blind studies. *JAMA* 1996;275:1507-13.
20. Dawber TR, Meadors GF, Moore FE Jr. Epidemiological approaches to heart disease: the Framingham Study. *Am J Public Health* 1951;41:279-81.
21. Kannel WB, Feinleib M, McNamara PM, Garrison RJ, Castelli WP. An investigation of coronary heart disease in families: the Framingham Offspring Study. *Am J Epidemiol* 1979;110:281-90.
22. Casale PN, Devereux RB, Alonso DR, Campo E, Kligfield P. Improved sex-specific criteria of left ventricular hypertrophy for clinical and computer interpretation of electrocardiograms: validation with autopsy findings. *Circulation* 1987;75:565-72.
23. Casale PN, Devereux RB, Kligfield P, et al. Electrocardiographic detection of left ventricular hypertrophy: development and prospective validation of improved criteria. *J Am Coll Cardiol* 1985;6:572-80.
24. Liang K-Y, Zeger SL. Longitudinal data analysis using generalized linear models. *Biometrika* 1988;73:13-22.
25. D'Agostino RB, Lee ML, Belanger AJ, Cupples LA, Anderson KA, Kannel WB. Relation of pooled logistic regression to time dependent Cox regression analysis: the Framingham Heart Study. *Stat Med* 1990;9:1501-15.
26. Kannel WB, Wolf PA. Inferences from secular trend analysis of hypertension control. *Am J Public Health* 1992;82:1593-5.
27. Sytkowski PA, D'Agostino RB, Belanger AJ, Kannel WB. Sex and time trends in cardiovascular disease incidence and mortality: the Framingham Heart Study, 1950-1989. *Am J Epidemiol* 1996;143:338-50.
28. Sprafka JM, Burke GL, Folsom AR, Luepker RV, Blackburn H. Continued decline in cardiovascular disease risk factors: results of the Minnesota Heart Survey, 1980-1982 and 1985-1987. *Am J Epidemiol* 1990; 132:489-500.
29. Kuczmarski RJ, Flegal KM, Campbell SM, Johnson CL. Increasing prevalence of overweight among US adults: the National Health and Nutrition Examination Surveys, 1960 to 1991. *JAMA* 1994;272:205-11.
30. Pringle SD, Macfarlane PW, McKillop JH, Lorimer AR, Dunn FG. Pathophysiologic assessment of left ventricular hypertrophy and strain in asymptomatic patients with essential hypertension. *J Am Coll Cardiol* 1989;13:1377-81.
31. Ghali JK, Kadakia S, Cooper RS, Liao YL. Impact of left ventricular hypertrophy on ventricular arrhythmias in the absence of coronary artery disease. *J Am Coll Cardiol* 1991;17:1277-82.
32. McLenachan JM, Henderson E, Morris KI, Dargie HJ. Ventricular arrhythmias in patients with hypertensive left ventricular hypertrophy. *N Engl J Med* 1987;317:787-92.
33. Lanti M, Puddu PE, Menotti A. Voltage criteria of left ventricular hypertrophy in sudden and nonsudden coronary artery disease mortality: the Italian section of the Seven Countries Study. *Am J Cardiol* 1990;66:1181-5.
34. Van Hoof R. Left ventricular hypertrophy in elderly hypertensive patients: a report from the European Working Party on High Blood Pressure in the Elderly trial. *Am J Med* 1991;90:Suppl 3A:55S-59S.
35. Verdecchia P, Schillaci G, Borgioni C, et al. Prognostic significance of serial changes in left ventricular mass in essential hypertension. *Circulation* 1998;97:48-54.
36. Morbidity and mortality: 1998 chartbook on cardiovascular, lung, and blood diseases. Rockville, Md.: National Heart, Lung, and Blood Institute, 1998.
37. Feinleib M, Pinsky J. Nonrandom attrition in the Framingham Heart Study: application: age trends in blood pressure. In: Dwyer JH, Feinleib M, Lippert P, Hoffmeister H, eds. *Statistical models for longitudinal studies of health*. Vol. 16 of Monographs in epidemiology and biostatistics. New York: Oxford University Press, 1992:16:261-76.
38. 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. [Erratum, *JAMA* 1992;268:3201.]