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Hemodynamic Patterns of Age-Related Changes in Blood Pressure: The Framingham Heart Study

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Abstract

Background: We attempted to characterize age-related changes in blood pressure in both normotensive and untreated hypertensive subjects in a population-based cohort from the original Framingham Heart Study and to infer underlying hemodynamic mechanisms.

Methods and Results: A total of 2036 participants were divided into four groups according to their systolic blood pressure (SBP) at biennial examination 10, 11, or 12. After excluding subjects receiving antihypertensive drug therapy, up to 30 years of data on normotensive and untreated hypertensive subjects from biennial examinations 2 through 16 were used. Regressions of blood pressure versus age within individual subjects produced slope and curvature estimates that were compared with the use of ANOVA among the four SBP groups. There was a linear rise in SBP from age 30 through 84 years and concurrent increases in diastolic blood pressure (DBP) and mean arterial pressure (MAP); after age 50 to 60 years, DBP declined, pulse pressure (PP) rose steeply, and MAP reached an asymptote. Neither the fall in DBP nor the rise in PP was influenced significantly by removal of subsequent deaths and subjects with nonfatal myocardial infarction or heart failure. Age-related linear increases in SBP, PP, and MAP, as well as the early rise and late fall in DBP, were greatest for subjects with the highest baseline SBP; this represents a divergent rather than parallel tracking pattern.

Conclusions: The late fall in DBP after age 60 years, associated with a continual rise in SBP, cannot be explained by "burned out" diastolic hypertension or by "selective survivorship" but is consistent with

increased large artery stiffness. Higher SBP, left untreated, may accelerate large artery stiffness and thus perpetuate a vicious cycle. (Circulation. 1997;96:308-315.)

Key Words: blood pressure, hypertension, aging, epidemiology, physiology.

Selected Abbreviations and Acronyms

BMI = body mass index

CHF = congestive heart failure

DBP = diastolic blood pressure

MAP = mean arterial pressure

MI = myocardial infarction

PP = pulse pressure

SBP = systolic blood pressure

There is a progressive increase in blood pressure with aging in industrialized societies, beginning in childhood and continuing into adulthood. [1-4] This trend is associated with a greater increase in SBP than DBP during the middle adult years. Whereas SBP continues to rise until the eighth or ninth decade, DBP tends to remain constant or decline after the fifth or sixth decade; as a consequence, PP increases progressively with age and the rate of rise accelerates after age 50 years. There also is a sex difference in blood pressure trends; women's blood pressure starts lower than men's, catches up by the sixth decade, and frequently becomes slightly higher thereafter. The majority of studies demonstrating age-related blood pressure changes in populations have been cross-sectional [4]; however, two longitudinal studies have reported the same pattern. [1,3]

What remains unclear, however, are the hemodynamic factors responsible for the age-related changes in blood pressure. The Framingham Heart Study provides a unique opportunity to observe the effects of aging on untreated blood pressure in a population-based cohort. This study began in 1948, long before the efficacy of treating mild and moderate hypertension had been established; only a minority of hypertensive participants of the original Framingham cohort were receiving antihypertensive therapy until the 1980s, [5] and these treated subjects were excluded from our analysis.

Previous Framingham publications have emphasized the increase in prevalence of hypertension with advancing age and the predominance of systolic hypertension in the elderly. [6,7] The goals of the present investigation were (1) to identify, in both normotensive and untreated hypertensive subjects, age-related changes in SBP, DBP, PP, and MAP, and (2) to infer alterations in hemodynamics based on longitudinal changes in blood pressure components.

Methods

Overview

The Framingham Heart Study began in 1948 with the enrollment of 5209 men and women, 28 to 62 years of age at entry, with all subjects undergoing biennial examinations. Each examination included an extensive cardiovascular history and physical examination, 12-lead ECG, and various blood chemistries. Morbidity and mortality were continuously monitored by biennial clinic examinations and by communication with physicians and relatives. All new cardiovascular events were reviewed by a panel of three experienced investigators. Detailed descriptions of study design and of end points for coronary heart disease have been published elsewhere. [8-10]

Study Population

The sample analyzed for this report included individuals who had Framingham measurements of HDL cholesterol as part of a complete lipid profile and also had no clinical evidence of coronary heart disease. The earliest available examination at which HDL cholesterol was measured served as the index examination for each subject; usually this was the 11th biennial examination but for some it was the 10th or 12th. These subjects have been investigated in an ongoing follow-up study. In addition, the population studied in the present investigation met the following criteria: (1) all participants were between the ages of 50 and 79 years at the index examination; (2) they were not receiving antihypertensive medication at baseline or before baseline; and (3) they had four or more examinations (from examinations 2 through 16) at which untreated blood pressure levels were measured. The mean number of biennial measurements of untreated blood pressure per subject was 12.3.

Of the original 5209 cohort participants, 780 died before the index examination, 676 did not attend a biennial examination during the prescribed period, and 877 did not receive a full lipid profile. Also excluded were 329 subjects because of clinically apparent coronary disease, 335 for receiving antihypertensive therapy, 95 for loss to follow-up, 48 because of insufficient data collection, and 33 because of age exclusion (< 50 or > 79 years).

Blood Pressure Measurement

Readings of SBP and DBP were taken in the supported left arm of the seated subject with the use of a mercury column sphygmomanometer with cuff-size adjustment made on the basis of arm circumference. Readings were recorded to the nearest even number. The SBP was recorded at the first appearance of Korotkoff sounds, and the palpitatory method was used to check auscultatory systolic readings. The DBP was recorded at the disappearance (phase V) of Korotkoff sounds. Determinations of SBP and DBP were based on the average of two separate measurements taken by the examining physician at each examination; however, if only one reading was recorded, its value was used.

Data Analysis

The sample used in this study consisted of 2036 subjects (890 men and 1146 women). These individuals were then divided into four groups (Table 1) according to recorded SBP at the index examination: group 1, < 120 mm Hg; group 2, 120 to 139 mm Hg; group 3, 140 to 159 mm Hg; and group 4, >or= to 160 mm Hg. By use of the new classification of hypertension, based on the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure (JNC V), group 1 consisted of "optimal" SBP; group 2, normal and high normal SBP; group 3, stage 1 systolic hypertension; and group 4, stages 2, 3, and 4 systolic hypertension. [11] SBP, DBP, PP, and MAP were obtained from biennial examinations 2 (antecedent) to 16 (subsequent). PP was defined as PP = SBP-DBP, and MAP was calculated from the standard equation MAP = (2/3)DBP + (1/3)SBP (in mm Hg). Values from the first biennial examination were not used because both SBP and DBP on that examination were generally higher than recorded on subsequent examinations. This finding was consistent with regression to the mean or a first-visit "white coat" hypertensive effect.

	Group 1	Group 2	Group 3	Group 4	P (Across Groups)
Defined SBP, mm Hg	<120	120-139	140-159	≥160	. . .
No. of subjects	456	833	515	232	. . .
Mean age, y	56.3	58.6	61.7	63.6	.001
Sex, % women	64.7	51.0	56.7	57.8	.001
Mean blood pressure, mm Hg					
SBP*	110	129	147	173	<.001
DBP*	70	78	84	91	<.001
Body height, in*	64.3	64.9	64.3	64.3	.002
BMI*	25.0	25.9	26.6	27.3	<.001
Total cholesterol*	230.3	230.0	232.8	231.6	.663
Smokers, %	45.4	40.5	36.0	34.0	.005
Diabetes mellitus, %	3.5	6.7	9.8	15.6	.001
Left ventricular hypertrophy (ECG), %	0.4	0.7	1.7	6.0	.001
Claudication, %	1.3	1.3	2.9	3.4	.053
Stroke, %	1.1	1.8	2.9	4.3	.029

*Age-adjusted by ANCOVA.

Table 1. Selected Clinical Characteristics by Systolic Blood Pressure Groups

In the analysis of selected clinical characteristics by SBP groups, the chi squared test was used to compare distributions of categorical variables. ANCOVA, after adjustment of baseline data for age, was used to compare means of continuous variables.

Initially, to provide an overview of arterial pressure relations with age, all available data within each given age interval (ages 30 to 34 through 80 to 84) on each arterial pressure component were averaged, by index examination SBP groupings from biennial examinations 2 to 16, as available, for all subjects. Thus, each subject contributed up to 15 examinations with blood pressure values recorded before and after the index examination. These analyses of group averaged data were conducted for the entire study cohort and again after excluding post-index examination deaths and subjects with nonfatal MI or CHF to evaluate for effects of possible "selective survivorship."

To determine if age-related patterns in blood pressure slope or curvature differed by SBP groupings, least-squares regression equations [12] were obtained for each subject, with the use of linear and quadratic terms for age, adjusted to an intercept estimated at age 60 years. One-way ANOVA [13] was used to compare means of slopes and curvatures among SBP groupings. These analyses were done for the entire cohort, separately for men and women. SAS statistical software (SAS Institute, Cary, NC) [14] was used. A value of $P < .01$ was considered significant.

Results

The SBP groupings of normotensive and untreated hypertensive subjects with various clinical characteristics are detailed and compared in Table 1. On the basis of index examination SBP values, 37% of subjects had hypertension (groups 3 and 4), 41% had normal or high normal blood pressure (group 2), and 22% had optimal blood pressure (group 1). Groups 3 and 4 were composed of 61% isolated systolic hypertension as defined by DBP < 90 mm Hg and SBP >or= to 140 mm Hg; 39% had combined systolic-diastolic hypertension as defined by DBP >or= to 90 mm Hg and SBP >or= to 140 mm Hg. Approximately one third of subjects with isolated systolic hypertension had a DBP >or= to 90 mm Hg at any examination before their index examination. Women made up 62% of subjects with isolated systolic hypertension and 47% of those with combined systolic-diastolic hypertension. As expected, there was a direct correlation between SBP groupings and BMI, diabetes mellitus, left ventricular hypertrophy by ECG, claudication, and stroke. There were no clinically significant correlations between body height, total cholesterol, and SBP groupings. Smoking was inversely related to both SBP groupings and BMI.

Group Averages

Arterial pressure components by age, representing group averages, are shown in Figure 1 (thick line) for all available data from each subject classified into 5-year age intervals (30 to 34 through 80 to 84) and classified by index examination SBP groups 1 through 4. The SBP patterns showed a consistent linear rise with aging in all four groups. The DBP patterns showed a significant early rise and late fall with a transition around age 50 to 60 years. Both normotensive subjects (groups 1 and 2) and hypertensive subjects (groups 3 and 4) displayed this early rise and late fall in the DBP. The PP showed a small early rise and an accelerated late rise in all groups. Since PP is increased by bradycardia, heart rates were compared within and between groups. There was a significant increase in heart rate, after sex and age correction, in SBP groups 1 through 4; the values were 72.7, 75.0, 77.5, and 80.5 bpm, respectively (P = .0001). In contrast, there were no significant changes in heart rates within SBP groups from the fourth to the ninth decades. Examination of the MAP pattern showed an early linear rise peaking around age 50 or 60 years, with groups 3 and 4 showing a small decline by the seventh to ninth decades. When 683 post-index examination deaths and subjects with nonfatal acute MI or CHF were excluded, a reanalysis of the remaining 1353 subjects showed essentially unchanged patterns for all four arterial components including the rise and fall in DBP (Figure 1, thin line).

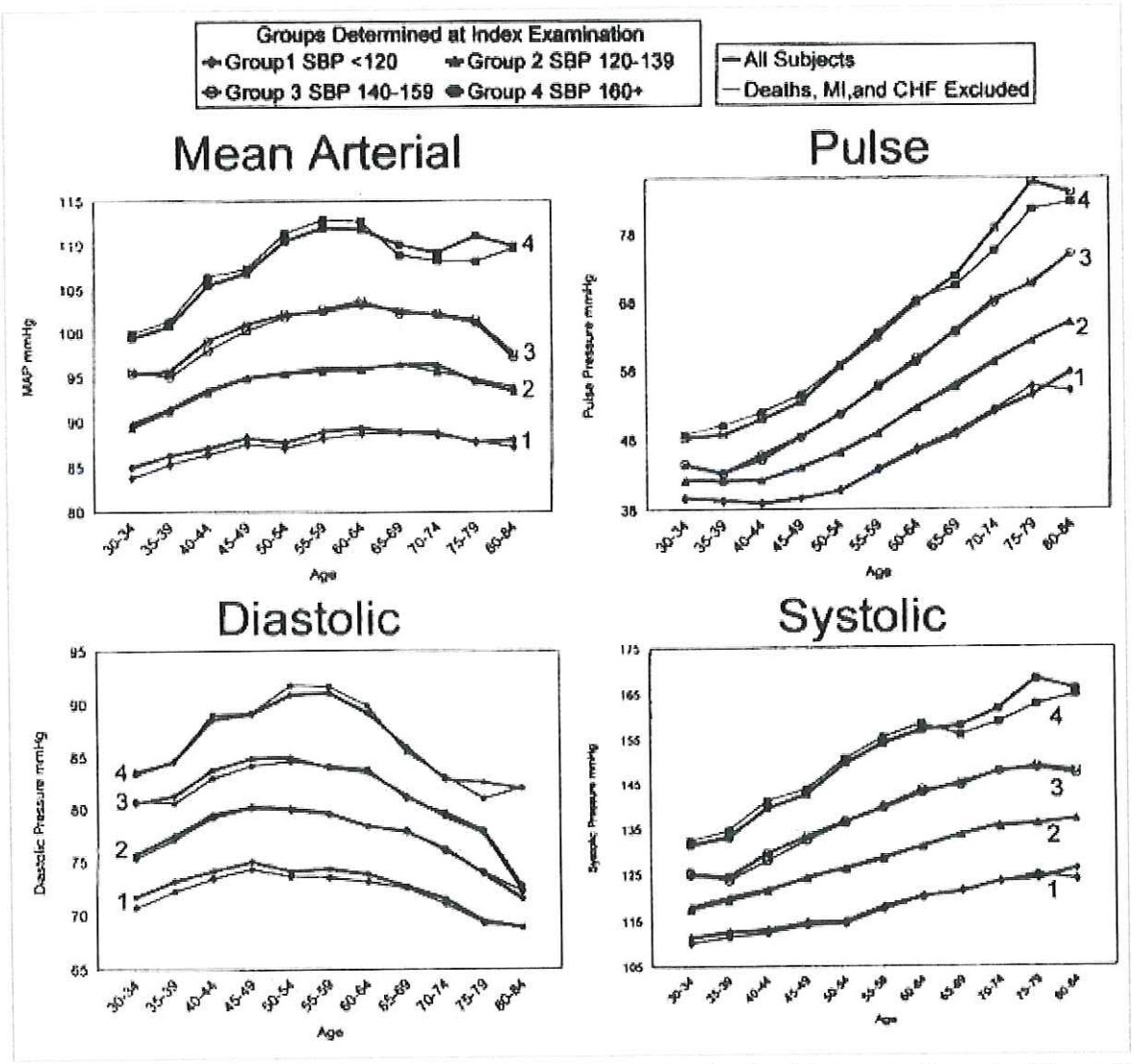

Figure 1. Arterial pressure components by age: Group averaged data for all subjects and with deaths, MI, and CHF excluded. Averaged blood pressure levels from all available data from each subject within 5-year age intervals (30 to 34 through 80 to 84) by SBP groupings 1 through 4. Thick line represents entire study cohort (2036 subjects); thin line represents study cohort with deaths and nonfatal MI or CHF excluded (1353 subjects).

Sex Differences

(Figure 2) shows group averaged data by sex for groups 1 and 4 for comparison of differences between the highest and lowest SBP groupings. There was a lower SBP in women than in men at the fourth decade by 13 to 14 mm Hg in group 4 and 3 to 4 mm Hg in group 1; this sex difference gradually narrowed and disappeared by the end of the seventh decade and reversed by the eighth decade, with women having a 4 to 5 mm Hg greater SBP than men in both groups 4 and 1. For DBP, group 4 women had an 8 to 9 mm Hg and group 1 women had a 2 to 3 mm Hg lower value than men in the fourth decade; these differences disappeared by the end of the seventh decade. Women had a slightly lower PP than men in the fourth decade by 4 to 5 mm Hg in group 4 but no difference in group 1; this sex difference gradually narrowed and then reversed by the seventh decade. By the ninth decade, women had a 6 to 7 mm Hg greater PP than men in group 4 and a 2 to 3 mm Hg greater PP in group 1 subjects. Women had a lower MAP than men in the fourth decade by 10 to 11 mm Hg in group 4 and a 3 to 4 mm Hg difference in group 1; this sex difference gradually narrowed and disappeared by the end of the seventh decade.

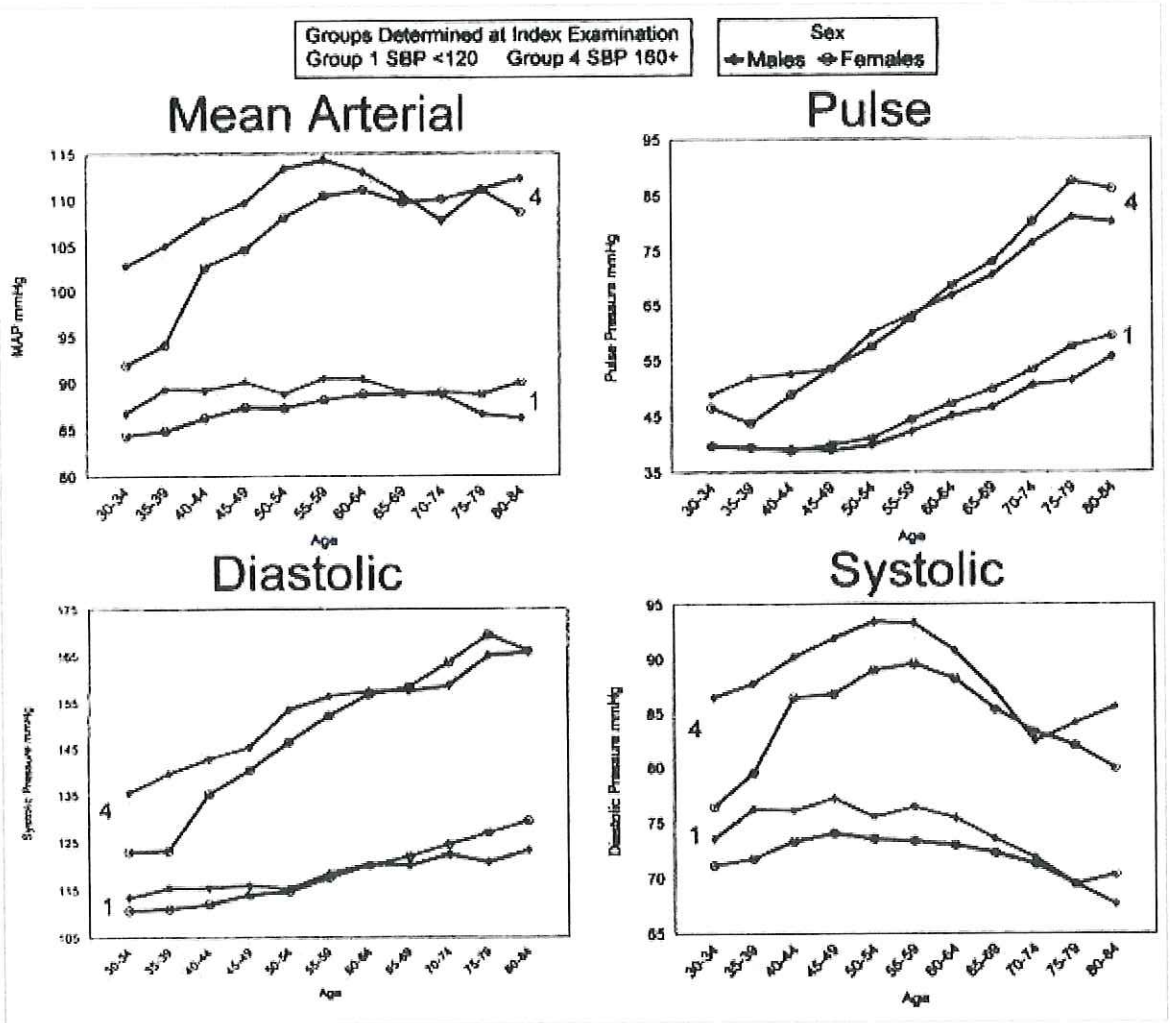

Figure 2. Arterial pressure components by age: Group averaged data by sex. Averaged blood pressure levels from all available data for each subject within 5-year age intervals (30 to 34 through 80 to 84) by SBP groupings 1 vs 4.

Individual Regression Analysis

Intergroup comparisons of slopes and curvatures for arterial pressure components by age and sex from ANOVA are shown in Table 2. Figure 3 presents plots of smoothed blood pressure variables by index SBP groups derived from the coefficients in Table 2. SBP slopes increased significantly from group 1 to group 4 ($F = 34.1$, $P < .001$) and differed significantly between all SBP group pairings ($P < .001$) with the exception of group 1 versus group 2 (not significant). Curvature coefficients for SBP were small, and there were few significant differences among groups, indicating that the association of SBP with age was linear. DBP curvatures but not slopes showed a significant increase across index examination SBP groupings in pooled sex analysis ($F = 5.5$, $P < .001$); in addition, there were significant differences in curvature between normotensive groups 1 and 2 and hypertensive groups 3 and 4 ($P < .01$) except between group 2 and group 4 ($P = .07$). Comparisons of PP slopes showed an increase by SBP groups ($F = 38.8$, $P < .001$), with highly significant differences ($P < .001$) between nearly all group pairings; PP curvatures differed much less among groups. Comparisons of the MAP slopes showed a significant increase across all four groups ($F = 16.3$, $P < .01$) and between all group pairs ($P < .01$), with the exception of group 1 versus group 2 (NS); MAP curvatures differed to a lesser extent.

		Estimated Coefficients for Group*				Group Pairwise Estimate					
	Overall *F*	1	2	3	4	1-2	1-3	1-4	2-3	2-4	3-4
SBP											
Slope											
Overall	34.1‡	.57	.75	1.18	1.97	.09	<.001	<.001	<.001	<.001	<.001
Male	25.3‡	.47	.61	1.22	2.29	.44	<.001	<.001	<.001	<.001	<.001
Female	11.9‡	.62	.89	1.14	1.73	.06	<0.01	<.001	.08	<.01	.003
Curvature											
Overall	1.6	.013	.007	.001	.013	.31	<.05	.96	.22	.46	.12
Male	2.7†	.014	.006	−.006	.025	.034	<.05	.38	.17	.07	<.01
Female	0.38	.013	.009	.006	.004	.65	.39	.37	.63	.55	.83
DBP											
Slope											
Overall	2.6	.19	.17	.11	.02	.77	.23	.01	.28	.01	.11
Male	3.6†	−.21	−.26	−.13	.12	.65	.44	.01	.15	.001	.05
Female	0.61	−.18	−.10	−.10	−.06	.28	.34	.25	.97	.71	.70
Curvature											
Overall	5.5‡	−.007	−.011	.019	−.018	.17	<.001	.008	.006	.066	.83
Male	3.1†	−.005	−.010	−.021	−.011	.27	.04	.37	.02	.91	.13
Female	3.6†	−.008	−.012	−.018	−.024	.34	.02	.004	.13	.02	.28
PP											
Slope											
Overall	38.8‡	.76	.93	1.29	1.95	.057	<.001	<.001	<.001	<.001	<.001
Male	22.2‡	.68	.86	1.35	2.17	.23	<.001	<.001	<.001	<.001	<.001
Female	17.2‡	.80	.99	1.24	1.78	.08	<.001	.016	<.001	<.001	<.001
Curvature											
Overall	1.68	.020	.019	.020	.031	.73	.99	.07	.73	.027	.066
Male	1.88	.019	.016	.015	.036	.66	.65	.09	.93	.02	.03
Female	0.32	.021	.021	.024	.027	.93	.63	.38	.66	.40	.63
MAP											
Slope											
Overall	16.3‡	.06	.13	.32	.67	.29	<.001	<.001	.006	<.001	<.001
Male	14.9‡	.016	.033	.32	.85	.88	.01	<.001	.003	<.001	<.001
Female	4.69‡	.087	.233	.31	.54	.11	.02	<.001	.37	.01	.08
Curvature											
Overall	3.54†	.002	.0049	.012	.008	.19	.002	.114	.025	.50	.34
Male	3.25†	.002	−.005	−.016	−.001	.25	.006	.95	.03	.37	.02
Female	1.99	−.001	.005	−.010	−.015	.43	.08	.03	.26	.10	.46

Slope and quadratic term (curvature) estimates for each blood pressure grouping, overall and by sex, averaged from individual least-squares regressions, with intercept based on predicted blood pressure at age 60 years. Overall *F* represents test of hypothesis of no difference across all blood pressure groupings, and group pairwise comparisons represent probability values for tests comparing slopes or curvatures between individual blood pressure groupings.

*Estimated change in SBP per year of increase in age defines slope; estimated change in SBP change per year defines curvature.

†$P<.05$; ‡$P<.001$.

Table 2. ANOVA Comparing Regression Lines of Each Blood Pressure Component With Age, Between SBP Groups, Overall Cohort, and by Sex

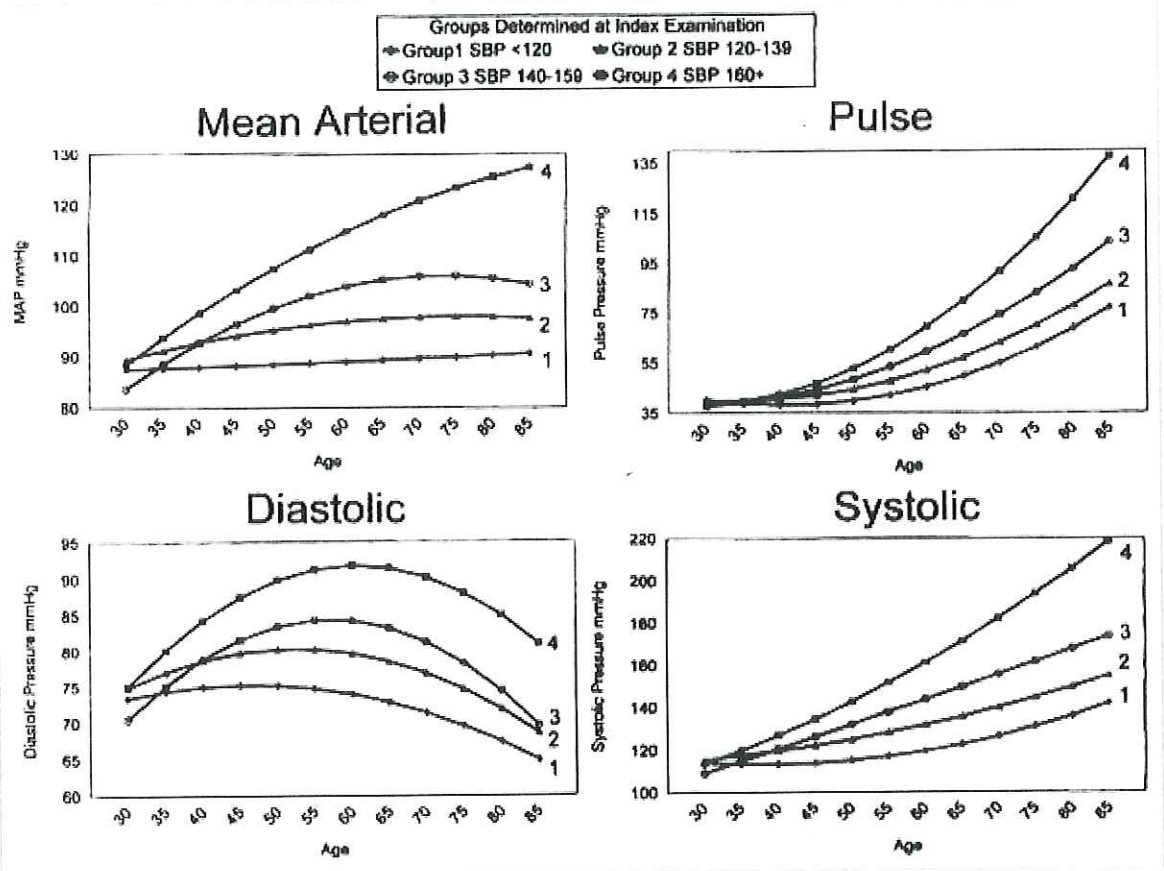

Figure 3. Arterial pressure components by age: Group averaged individual regression analysis. Curves plotted based on blood pressure predicted values at 5-year age intervals (age, 30 to 85 years) from least-squares regression equations, developed from individual intercept, slope, and quadratic term (curvature) coefficients averaged from individual least-squares mean regressions of each arterial pressure component by age.

Discussion

The normotensive and untreated hypertensive subjects in this study showed a linear rise in SBP from age 30 through 84 years and a concurrent early increase in DBP and MAP; after age 50 to 60 years, DBP declined, PP rose steeply, and MAP reached an asymptote. Analysis of individual subject regressions as a function of index examination SBP groups showed that linear slopes differed for SBP, PP, and MAP, whereas it was curvature that differed for DBP; these represented divergent rather than parallel tracking patterns.

The age-related late fall in DBP, as noted in previous cross-sectional studies and in the present investigation, has not been adequately explained. The reduction of DBP after age 60 years has been attributed to "burned out" diastolic hypertension, [15] but this decrease in DBP was observed in both normotensive and untreated hypertensive individuals, making it unlikely that "burned out" diastolic hypertension could explain the decreasing DBP in the elderly. Furthermore, only about one third of subjects with isolated systolic hypertension in groups 3 and 4 had an elevated DBP at an examination before the index visit. Similarly, the concept of "selective survivorship," whereby vulnerable patients are eliminated because of premature death, has been postulated as a cause of the late decline in DBP. Again, when all deaths and patients with nonfatal MI or CHF were removed from the study sample, the late fall in DBP was still present, making "selective survivorship" an unlikely explanation. A further hypothesis, namely an age-related decrease in cardiac output as the cause for the late fall in DBP, is inconsistent with the late rise in SBP. The most likely explanation, therefore, for the fall in DBP after age 60 years is increased large artery stiffness. [16-21]

The decline in DBP seen in the elderly is probably the result rather than the cause of the disease process. Age-related stiffening of the aorta is associated with a decreased capacity of the elastic reservoir and hence a greater peripheral runoff of stroke volume during systole. Thus, with less blood remaining in the aorta at the beginning of diastole, and with diminished elastic recoil, diastolic pressure decreases with increased steepness of diastolic decay. [22] The exaggerated fall in DBP seen in elderly hypertensive subjects suggests a process of transmural pressure-induced arterial wall damage resulting in large artery stiffness. [16,23]

The steep rise in PP after the sixth decade, in part secondary to the fall in DBP, cannot be due to elevated cardiac output or bradycardia, since studies in elderly hypertensives have shown a reduction in cardiac output at rest, [24,25] and we found a significant stepwise increase in heart rate with rising SBP in the present analysis. The rise in heart rate, as noted in SBP groups 1 through 4, would decrease rather than increase PP. The most plausible explanation for both the late rise in PP and the fall in DBP is an increase in large artery stiffness caused by intrinsic structural abnormalities. The pathological processes of thinning, fragmentation, and eventual fracturing of elastin and increased collagen and calcium deposition in the large arteries are likely explanations. [18,26-28]

Calculated MAP is used commonly as an approximation of vascular resistance when cardiac output is not elevated. [19,20] However, the leveling off of MAP after age 50 to 60 years in all SBP groups in the present study suggests that vascular resistance is underestimated in older persons, since there is firm evidence that vascular resistance continues to rise with aging. [24,29-32] True vascular resistance is underestimated by the MAP equation in part because aging alters the pulse wave contour, such that the standard form factor of 0.33 becomes closer to 0.5 (a sign-wave pattern). [18] In addition, if the rate of fall in DBP is substantial, as seen in hypertensive SBP groups 3 and 4, the calculated MAP actually decreases after the seventh or eighth decade (Figure 1), further contributing to underestimation of vascular resistance. Clearly, after age 50 years, the MAP equation is no longer a surrogate measurement for vascular resistance.

The present study supports the concept of an interaction between aging and hypertension in the progressive fall of DBP and rise of SBP. Group 1, with the lowest index SBP, had no early rise in PP and only a minimal early increase in MAP with age (Figure 1). Nevertheless, group 1 showed a significant rise in PP and fall in DBP after age 60 years, presumably caused by an increase in large artery stiffness secondary to aging in these initially normotensive subjects (mean index blood pressure of 111/70). In contrast, group 4, with high baseline SBP (mean index blood pressure of 173/90), showed both a significantly steeper rise in PP and a fall in DBP after age 60 than was observed in group 1 subjects. These findings suggest a linkage between hypertension left untreated and subsequent late acceleration of large artery stiffness. This in turn may perpetuate a vicious cycle of accelerated rise in SBP and a further increase in large artery stiffness.

Age-related blood pressure changes were generally similar in both sexes, but as noted in previous studies, young women had lower blood pressure values than similarly aged men; these differences gradually narrowed and eventually reversed beyond age 60 years. The lower blood pressure in young women compared with young men has been explained by their shorter stature; blood pressure amplification from central to peripheral arteries increases with body height and is therefore more marked in men. [33] Sex differences in blood pressure were more marked in hypertensive subjects. These findings suggest that there may be sex differences in arterial stiffening, with young women having more compliant vessels. With the onset of menopause this difference may be lost, with a resulting acceleration in arterial stiffening. [34,35]

Alterations in hemodynamics, in the absence of direct measurements, can be inferred by means of longitudinal changes in blood pressure variables as assessed in the present study. Arterial pressure can be divided into steady (MAP) and pulsatile components (PP). [16-19] MAP is determined by cardiac output and vascular resistance. The PP component, representing the variation in pressure around the mean, is influenced by left ventricular ejection, large artery stiffness, early pulse wave reflection, and heart rate. Both increased resistance and increased stiffness elevate SBP. In contrast, DBP rises with increased resistance but falls with increased stiffness; the relative contribution of each determines the ultimate DBP. [16-21] Therefore, age-related changes in SBP and DBP may predict the relative contributions of vascular resistance and large artery stiffness.

The hemodynamic significance of the rises in MAP, SBP, and DBP from age 30 to 49 years in the present study is consistent with a gradual increase in peripheral vascular resistance with aging. [19] Increased cardiac output appears to produce similar changes in these arterial pressure components. However, the transitory increase in cardiac output observed in some hypertensive young adults reverts over time into a persistent increase in vascular resistance. [36] Therefore, the slowly progressive increases in MAP, SBP, and DBP, noted in both normotensive and untreated hypertensive Framingham subjects from age 30 to 49, most likely result from increased peripheral vascular resistance.

The pulsatile component of arterial pressure (PP) varies with age. During the fourth and fifth decades we found that the increase in PP was small and correlated with the rise in MAP in groups 1 through 4 (Figure 1). This could be explained by a "downstream" increase in vascular resistance causing an "upstream" increase in transmural pressure, which in turn chronically stretched large central arteries and increased their stiffness.

There is strong evidence that vascular resistance is not the dominant factor in the rise in SBP after age 60 years. While measurements of cardiac output and blood pressure suggest increased vascular resistance with aging, [29,30] total peripheral resistance is only marginally elevated in older subjects with isolated systolic hypertension compared with age- and sex-matched normotensive control subjects. [24,31] Furthermore, studies of elderly subjects with isolated systolic hypertension showed that increased input impedance (large artery stiffness and early pulse wave reflection) predominated over increased vascular resistance. [32] In addition, a computer simulation of a modified Windkessel model for geriatric isolated systolic hypertension indicated that vascular resistance increased by only 25%, whereas there was a 50% to 75% increase in input impedance secondary to large artery stiffness and early wave reflection. [37] These conclusions are further supported by the observed decrease in DBP and increase in SBP after age 60 in the Framingham subjects.

The age-related linear rise in SBP from age 30 to 84 years, coupled with an early rise and late fall in DBP, suggests three hemodynamic phases. Under age 50, the progressive rise in DBP suggests the predominance of increased vascular resistance. The constancy of DBP during the 50s, together with the asymptotic leveling of MAP and increased slope of PP, suggests that increased vascular resistance and large artery stiffness are both increasing in a parallel manner. The fall in DBP during the later ages signals a preponderance of large artery stiffness as the cause of further rise in SBP in the elderly.

The strengths of this investigation, compared with previous longitudinal studies of age-related changes in blood pressure, [1,3] are the elimination of treated hypertensive subjects from the analysis, the greater number of interval examinations (up to 16 per subject), and the tracking of age-related blood pressure patterns by normotensive and hypertensive SBP groupings.

There are potential limitations in the present study. Since the original Framingham population consisted of > 99% Caucasians, the majority of whom were middle-class subjects, results may not apply to other ethnic or socioeconomic groups. The defined population consisted of subjects with a minimum age of 30 years at entry. Therefore, the results do not apply to children, adolescents, or young adults. However, previous longitudinal studies of age-related blood pressure changes in the young have shown a strong correlation of age with MAP, SBP, and DBP. [38] There may have been a selection bias resulting from the exclusion of 335 subjects receiving antihypertensive therapy, which represented 30% of the hypertensive population in this study. Since elevated DBP was the main criterion for treating hypertension until the early 1980s, this may have resulted in a higher prevalence of isolated systolic hypertension in the present study. However, this selection process, by eliminating the most severe hypertensives on treatment, resulted in a study of normotensives and predominantly untreated stage 1 hypertension. The latter comprises [nearly =] 74% of hypertensives, as noted in population studies. [39] The conclusions regarding observed differences in blood pressure patterns with aging may in part be confounded by risk factors not adjusted for in the present analysis. However, the intent of this study was to identify age-related blood pressure changes in a population-based cohort; future studies will address possible etiologic factors.

Does the presence of pseudohypertension impose limits on the conclusions of this study? With the most careful cuff measurements, true SBP is underestimated by 0 to 5 mm Hg and true DBP overread by 5 to 15 mm Hg or more compared with simultaneous intra-arterial pressure recordings. [40] Although the DBP artifact may be present regardless of age or blood pressure level, this entity is found more frequently in elderly hypertensives with large artery stiffness. [40] If diastolic pseudohypertension is present and underdiagnosed in the current study, the risk markers of increased PP and decreased DBP would be biased toward the null. We conclude that diastolic pseudohypertension, if present, would lead to an underestimation of true large artery stiffness.

Summary

The early rise in MAP, SBP, and DBP, up to age 50 years, is consistent with increasing peripheral vascular resistance. The late fall in DBP after age 50 to 60, associated with a steep rise in PP, cannot be explained by "burned out" diastolic hypertension or by "selective survivorship" but is consistent with increased large artery stiffness. The linear rise in SBP seen with aging is due primarily to increased peripheral vascular resistance during the early years and to increased large artery stiffness during the late years. After age 50, there is a progressive underestimation of vascular resistance by the MAP equation, largely because of a changing contour in the arterial pulse wave and the declining DBP. Despite a probable further increase in vascular resistance with aging, downward movement in DBP indicates that large artery stiffness predominates.

The most important clinical implications that can be derived from this study are that after the sixth decade of life, (1) increasing PP and decreasing DBP are surrogate measurements for large artery stiffness; (2) large artery stiffness rather than vascular resistance becomes the dominant hemodynamic factor in both normotensive and hypertensive subjects; and (3) hypertension, left untreated, may accelerate the rate of development of large artery stiffness. This, in turn, can perpetuate a vicious cycle of accelerated hypertension and further increases in large artery stiffness. These factors should be considered in cardiovascular risk stratification of the elderly and in selection of treatment modalities.

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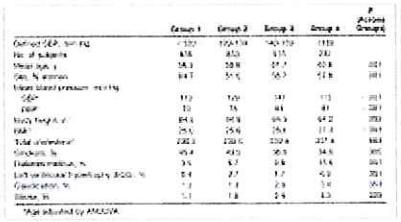

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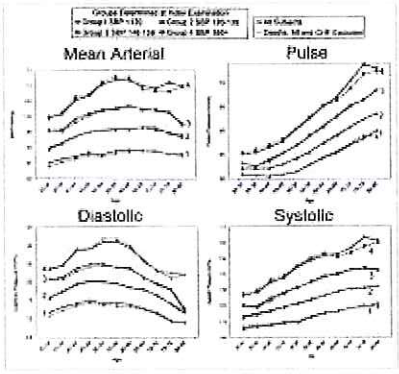

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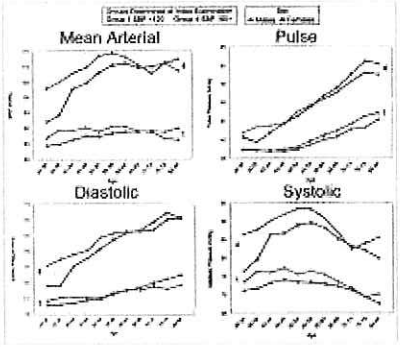

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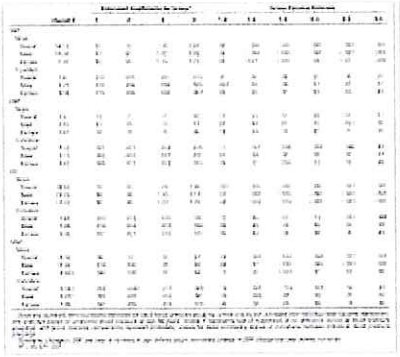

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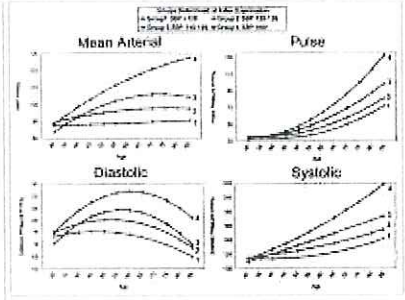

☐ Figure 3

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