Assessment of Aortic Line of Elasticity Using Polynomial Regression Analysis

Christodoulos Stefanadis, MD, FESC; John Dernellis, MD; Eleftherios Tsiamis, MD; Leonidas Diamantopoulos, MD; Andreas Michaelides, MD, FESC; Pavlos Toutouzas, MD, FESC

Background—The aim of this study was to assess the sigmoid line of elasticity in the human aorta.

Methods and Results—The pressure-diameter relation was measured in the descending aorta in 120 subjects. In an additional group of 6 subjects, transient vena caval occlusion produced 5 sets of pressure-diameter data. We found that the best fit curve of the pooled pressure-diameter data was a third-order polynomial. A polynomial equation was used to calculate the sigmoid line of elasticity in the entire population and after the administration of diltiazem (15 patients) or enalaprilat (10 patients). The sigmoid line of elasticity was significantly different with respect to age (P<0.001), history of hypertension (P<0.004), and hypercholesterolemia (P<0.02). The difference between the transition point and the peak systolic pressure was increased in normal subjects compared with patients (P<0.0001). The sigmoid line shifted leftward and upward with diltiazem, but it remained unchanged with enalaprilat. During an average of 3 years of follow-up, 19 of 88 patients developed stroke (n=4), unstable angina (n=8), acute myocardial infarction (n=4), or acute pulmonary edema (n=3).

Conclusions—This approach provides a quantitative evaluation of the aortic line of elasticity, which can differentiate the intrinsic from the extrinsic aortic elastic properties. Furthermore, it is a powerful and independent risk factor for cardiovascular events. (Circulation. 2000;101:1819-1825.)

Key Words: aorta ■ elasticity ■ nonlinear dynamics

The analysis of aortic function by the sigmoid curve of elasticity provides good differentiation of intrinsic aortic properties from extrinsic changes.1,2 Active changes in the elastic properties of the aorta are related to changes in the intrinsic elastic properties of the aorta and are characterized by the shifting of the pressure-diameter loop to a different line of elasticity. Passive changes in aortic elastic properties are characterized by the sliding of the pressure-diameter loop upward or downward along the same sigmoid line of elasticity.2

The purpose of the present study was to use pressure-diameter relationships to assess the aortic line of elasticity in humans. (1) We tested the best-curve fit to the pressure-diameter relation of the aorta over a physiological range of aortic pressures, which were modified by manipulating preload using transient inferior vena caval occlusion in 6 patients. (2) Using the analysis of nonlinear behavior of the thoracic aorta in 120 patients who underwent cardiac catheterization, we investigated the factors that influence the aortic curve of elasticity. (3) We calculated the transition point of the third-order polynomial and the relative position of each aortic loop on the aortic line of elasticity. (4) We studied the effects of diltiazem and enalaprilat on the sigmoid line of elasticity. (5) Finally, we examined the prognostic benefit of the aortic line of elasticity in predicting cardiovascular events in patients with hypertension, congestive heart failure, and coronary artery disease.

Methods

Study Population

A total of 120 patients were selected from those who were routinely referred to undergo cardiac catheterization at our institution. Of these patients, 49 had coronary artery disease, which was diagnosed by a positive result on coronary arteriography, and 28 had moderate or severe hypertension. The remaining 32 were normal subjects who underwent coronary angiography to evaluate symptoms compatible with angina pectoris.

In 25 of the hypertensive patients, the effects of vasodilating drugs (diltiazem or enalaprilat) on the aortic line of elasticity were studied. Eleven of these 120 patients had congestive heart failure (7 due to ischemic heart disease and 4 due to idiopathic dilated cardiomyopathy). We also examined 6 additional subjects (5 men and 1 woman) who had coronary artery disease (2 patients), congestive heart failure (1 patient), or hypertension (1 patient) or who were normal subjects (2 patients). In these 6 subjects, volume load was altered by transient inferior vena caval occlusion. All patients discontinued medications, if any, for $\geq5$ half-lives before the study, except for intravenous furosemide or sublingual nitroglycerine, which were given when indicated. The protocol was approved by the Institutional Ethics Committee of our institution, and all patients gave informed consent before participation.

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1819
Measurement of Diameter and Pressure
The aortic pressure-diameter relation was calculated as previously described.1–7

Protocol of Transient Vena Caval Occlusion
A balloon catheter (Balt, Cristal balloon valvuloplastie) was inserted via a femoral vein sheath. The balloon was gradually inflated in the right atrium and simultaneously and gently drawn back toward the inferior vena cava until it fit snugly at the right atrium and inferior vena caval junction. This maneuver led to a reproducible preload reduction; the fall in peak systolic pressure averaged 30%.8 After 8 to 10 s, the balloon was deflated, and venous return was allowed to recover. Heart rate changed by only 0 to 4 beats/min during the period in which pressure fell.

Administration of Vasodilating Drugs
In 15 patients, after baseline measurements, diltiazem was administered intravenously through a peripheral line in a bolus dose of 0.15 mg/kg over a period of 2 minutes.5 In another group of 10 age- and sex-matched hypertensive patients, enalaprilat was administered intravenously through a peripheral line in a bolus dose of 1.25 mg over a period of 5 minutes. Measurements were continuously monitored and recorded at baseline, at the end of drug administration, and repeatedly thereafter for 20 minutes.

Clinical and Laboratory Parameters
Left ventricular ejection fraction and mass index were calculated using 2D echocardiography (HP Sonos 2500). Hypertension history, smoking (>5 cigarettes per day), hyperlipidemia (total cholesterol >200 mg/dL), and diabetes mellitus (fasting serum level of glucose >100 mg/dL) were assumed as simple independent variables with 2 categories.

Data Analysis
The aortic pressure-diameter relation was obtained by plotting the diameter versus pressure of digitized data. We used a polynomial regression program (SPSS for Windows, version 8) to discover the best-fit curve. In the transient vena caval occlusion group, there were 5 cardiac cycles of different loading conditions. We performed the polynomial regression analysis starting with a first-order polynomial (linear) and then proceeded, one order at a time, to a third-order polynomial.9 We compared 2 models with the same number of parameters using the F ratio, as described in the Appendix. The fit with the lower residual SS was superior because its curve lay closer to the points. Then, we determined whether the 2 sets of data of the 2 sequential cardiac cycles differed significantly. This test was repeated for all sets of data for each patient. If a higher-order regression model that fit the 5 sets of data, which were analyzed separately, did not differ significantly, the same general model was used to fit the pooled (combined) sets of data when analyzed simultaneously (see Appendix). This polynomial describes the equation of the sigmoid line of elasticity.9 –11

The transition point is given by the following formula: $P_{\text{trans}} = -b_5 / 3b_6$. This formula results from the second derivative of the third-order polynomial, which is $F''(x) = 6b_5 x + 2b_6$. The point that zeroes the $F''(x)$ represents the pressure ($P_{\text{trans}}$) at which the aortic line of elasticity diverges due to changes in aortic elastic behavior. The position of the pressure-diameter relation on the aortic line of...
elasticity was estimated by the difference between $P_{\text{trans}}$ and peak systolic pressure ($P_{\text{dif}} = P_{\text{trans}} - \text{peak systolic pressure}$) in each patient.

### Definition of End Points

A total of 88 patients were followed-up for a mean period of 3 years; no patient was lost to follow-up. Information was obtained by reviewing hospital records, direct contact with the patient’s primary physician, or contact with the patient by means of a questionnaire. End points included hospitalization for stroke, unstable angina, acute myocardial infarction, or acute pulmonary edema. A cerebrovascular event was documented by a computed tomography scan and confirmed by a neurologist.

### Statistical Analysis

ANOVA and paired $t$ tests were used to compare continuous variables. Pair-wise comparisons between group means were done with the Bonferroni $t$ test. The linear regression lines of the 5 sets of data of the 6 patients who underwent vena caval occlusion were compared using ANCOVA. Multivariate analysis of variance for multiple dependent variables by additional factor variables or covariates was used to test the null hypothesis of the effects of age, body mass index, sex, coronary artery disease, left ventricular mass index, left ventricular ejection fraction, diabetes mellitus, hypercholesterolemia, smoking habit, and history of hypertension with the parameters ($b_0$, $b_1$, $b_2$, and $b_3$) of the polynomial equation, which were the dependent variables.

In addition, interactions between factors and the effects of individual factors were investigated. All statistical assumptions were met, and no multicollinearity problems existed our analysis. The probability of survival in various patient subgroups was estimated by the Kaplan-Meier method. Multivariate comparisons of the influence of the aforementioned factors on survival were performed using the Cox proportional hazard method. The cumulative hazard function, as well as the partial residuals and the differences in $b$ values for the covariates, were used to check the distribution and the proportionality of the hazard over time (SPSS-Save-Diagnostics). All assumptions were valid. Relative risk and 95% confidence limits were calculated from the proportional hazard model as parameter estimates. All tests were considered significant at $P = 0.05$.

### Results

#### Sigmoid Line of Elasticity

The analyses of the 5 cardiac beats in the vena caval occlusion group revealed that the linear regression lines were different in all patients (ANCOVA, with $P$ between 0.01 and

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**Table 1. Clinical Characteristics and Hemodynamic Data of All Subjects**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjects, n</td>
<td>120</td>
</tr>
<tr>
<td>Age, y</td>
<td>56.9±11.7</td>
</tr>
<tr>
<td>Sex, M/F</td>
<td>98/22</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>25.0±2.2</td>
</tr>
<tr>
<td>Smoking habit, n</td>
<td>23</td>
</tr>
<tr>
<td>Hypercholesterolemia, n</td>
<td>23</td>
</tr>
<tr>
<td>History of hypertension, n</td>
<td>43</td>
</tr>
<tr>
<td>Diabetes mellitus, n</td>
<td>23</td>
</tr>
<tr>
<td>Left ventricular mass index, g/m²</td>
<td>95.2±20.5</td>
</tr>
<tr>
<td>Left ventricular ejection fraction, %</td>
<td>51.6±10.6</td>
</tr>
<tr>
<td>Coronary artery disease, n (1-2-3 vessels)</td>
<td>49 (13-18-18)</td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>143.6±20.0</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg</td>
<td>102.6±15.8</td>
</tr>
<tr>
<td>Systolic diameter of aorta, mm</td>
<td>22.0±1.7</td>
</tr>
<tr>
<td>Diastolic diameter of aorta, mm</td>
<td>20.1±2.0</td>
</tr>
<tr>
<td>$b_0$</td>
<td>17.5±8.4</td>
</tr>
<tr>
<td>$b_1$</td>
<td>0.19±0.05</td>
</tr>
<tr>
<td>$b_2$</td>
<td>$-1.15\pm0.81\times10^{-3}$</td>
</tr>
<tr>
<td>$b_3$</td>
<td>$2.56\pm0.23\times10^{-6}$</td>
</tr>
<tr>
<td>$P_{\text{trans}}, \text{mm Hg}$</td>
<td>154.7±21.3</td>
</tr>
<tr>
<td>$P_{\text{dif}}, \text{mm Hg}$</td>
<td>11.1±3.4</td>
</tr>
</tbody>
</table>

Values are mean±SD or No. of patients. $b_0$, $b_1$, $b_2$, and $b_3$ are parameters of the cubic equation that express the aortic line of elasticity.

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**Table 2. Effects of Clinical and Laboratory Variables on the Aortic Line of Elasticity**

<table>
<thead>
<tr>
<th>Independent Factors or Covariates</th>
<th>Multivariate Tests of Significance</th>
<th>Univariate F Tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.001</td>
<td>0.001</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.004</td>
<td>0.001</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>0.02</td>
<td>0.01</td>
</tr>
<tr>
<td>Interactions</td>
<td></td>
<td>0.02</td>
</tr>
<tr>
<td>Age by Hypertension</td>
<td>0.03</td>
<td>0.03</td>
</tr>
</tbody>
</table>

$P$ values referred to the significance of the F test from the multivariate analysis of variance. All other independent variables did not show significant effects on the aortic line of elasticity.
The third-order regression model provided the best curve fit; its residual sum of squares (SS) was significantly less than that of the second-order polynomial for every beat in all patients (P between 0.01 and 0.001). Thus, the sigmoid line of elasticity is best described by the following equation: 

\[ D = b_0 + (b_1 P) + (b_2 P^2) + (b_3 P^3) \]

where P and D are the instantaneous aortic pressure and diameter, respectively, and \( b_0 \), \( b_1 \), \( b_2 \), and \( b_3 \) are the parameters of the polynomial. In each patient, the cubic regression lines of the 5 sets of data did not differ in the 2×2 comparison using the F test (P>0.05 for all comparisons). In Figure 1, the 5 sets of pressure-diameter data that were produced by transient vena caval occlusion are shown; the third-order regression line represents the sigmoid line of elasticity.

**Effects of Clinical and Laboratory Parameters on the Aortic Line of Elasticity**

In Table 1, the demographic data, clinical characteristics, and hemodynamic parameters of the subjects are shown. In the pooled population of 120 subjects, multivariate tests revealed that the sigmoid line of elasticity of the aorta was significantly different with respect to age, history of hypertension, and hypercholesterolemia, both in multivariate and univariate comparisons. In Table 2, significant interactions were found between variables (ANOVA, P<0.001; Figure 2). Pair-wise comparisons revealed that a significant difference existed between each pair (P<0.05), except for the pair of hypertensives versus patients with coronary artery disease (P=NS).

**Effect of Vasodilating Drugs on the Aortic Line of Elasticity**

No difference existed at baseline between the 2 subgroups of hypertensive patients who took either diltiazem or enalaprilat with respect to demographic and hemodynamic data. Diltiazem resulted in a significant upward and leftward shift of the aortic line of elasticity in all patients (Figure 3). Furthermore, the mean values of the polynomial parameters showed significant changes between groups (Table 3). Although the transition point did not change significantly, \( P_{\text{dif}} \) significantly increased (Table 3 and Figure 3). In contrast, the aortic line of elasticity did not alter in any patient after enalaprilat administration (Figure 4). The aortic loop slid downward along the same sigmoid line. Furthermore, no polynomial parameter showed significant changes during the time that \( P_{\text{dif}} \) was significantly increased (Table 4).

**Predictors of End Points**

During follow-up, 19 of 88 patients reached an end point. Of these 19 patients, 4 had hypertension and developed stroke; disease, and congestive heart failure (P<0.001). Nevertheless, the difference in pressure (\( P_{\text{dif}} \)) decreased with these variables (P<0.01). Moreover, \( P_{\text{dif}} \) was significantly different between groups of subjects (ANOVA, P<0.0001; Figure 2). Pair-wise comparisons revealed that a significant difference existed between each pair (P<0.05), except for the pair of hypertensives versus patients with coronary artery disease (P=NS).

**TABLE 3. Effects of Diltiazem on the Aortic Line of Elasticity in 15 Hypertensive Patients**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline</th>
<th>Diltiazem</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>176±6</td>
<td>160±11</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg</td>
<td>98±6</td>
<td>89±7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>( b_0 )</td>
<td>13.9±3.8</td>
<td>12.1±3.9</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>( b_1 )</td>
<td>0.19±0.03</td>
<td>0.25±0.03</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>( b_2 \times 10^{-3} )</td>
<td>-1.39±0.09</td>
<td>-1.52±0.13</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>( b_3 \times 10^{-6} )</td>
<td>2.48±0.11</td>
<td>2.71±0.12</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>( P_{\text{trans}} ), mm Hg</td>
<td>187±6</td>
<td>186±9</td>
<td>NS</td>
</tr>
<tr>
<td>( P_{\text{dif}} ), mm Hg</td>
<td>11±7</td>
<td>25±8</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

**TABLE 4. Effects of Enalaprilat on Aortic Line of Elasticity in 10 Hypertensive Patients**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline</th>
<th>Enalaprilat</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>180±15</td>
<td>156±15</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg</td>
<td>93±7</td>
<td>84±8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>( b_0 )</td>
<td>15.9±6.2</td>
<td>16.1±6.7</td>
<td>NS</td>
</tr>
<tr>
<td>( b_1 )</td>
<td>0.16±0.05</td>
<td>0.19±0.05</td>
<td>NS</td>
</tr>
<tr>
<td>( b_2 \times 10^{-3} )</td>
<td>-1.45±0.13</td>
<td>-1.46±0.15</td>
<td>NS</td>
</tr>
<tr>
<td>( b_3 \times 10^{-6} )</td>
<td>2.58±0.14</td>
<td>2.58±0.11</td>
<td>NS</td>
</tr>
<tr>
<td>( P_{\text{trans}} ), mm Hg</td>
<td>187±10</td>
<td>187±10</td>
<td>NS</td>
</tr>
<tr>
<td>( P_{\text{dif}} ), mm Hg</td>
<td>7±9</td>
<td>31±11</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>
12 had coronary artery disease and developed either unstable angina (n=8) or acute myocardial infarction (n=4); and 3 had congestive heart failure and developed acute pulmonary edema. The event-free survival rate at 59 months of follow-up was 73% (Figure 5). Specifically, the stroke-free survival rate in hypertensives was 79%; the acute coronary event–free survival rate in patients with coronary artery disease was 71%; and the acute pulmonary edema–free survival rate in patients with congestive heart failure was 70% (Figure 5). No patient died of a noncardiac cause. Multivariate Cox proportional hazards analysis revealed that the only independent predictors of risk of the multiple cardiovascular end points were the polynomial parameters of the aortic line of elasticity (b0, b1, b2, and b3), as well as Pdif (Table 5).

**Discussion**

There are 5 main findings in the present study. (1) The sigmoid line of elasticity of the human aorta was described in vivo; this line represents a third-order polynomial and, for the normal range of aortic pressures, it could be calculated from a single beat. This approach can differentiate the intrinsic from the extrinsic properties of the aorta. (2) Age, history of hypertension, and hypercholesterolemia affect the aortic line of elasticity; the impact of these clinical parameters is seen in the intrinsic elastic properties of the aorta. (3) The aorta operates at a point lower than the transition point in normal subjects, but in patients, the aorta functions near or above the transition point. (4) Vasodilating drugs have a differential effect on the aortic line of elasticity. Diltiazem shifts the aortic loop onto a different sigmoid line, whereas enalaprilat slides the aortic loop downward along the same sigmoid line of elasticity. (5) The parameters of the third-order polynomial and the position of the aortic loop on the aortic line of elasticity are independent predictors of cardiovascular events.

**Consideration of the Methods**

In this study, we showed that a nonlinear polynomial models the pressure-diameter relation of the aorta better than a linear one. Indeed, the third-order polynomial had a lower residual SS compared with the linear and second-order polynomial. Furthermore, the linear regression lines of the aortic loops during altered preload were significantly different while these loops lay on the same curve. Finally, Lanne et al12,13 also found that the aortic pressure-diameter curve is nonlinear, with one transition point. A curve with one transition point is described with a third-order polynomial.

**Transition Point**

The transition point should reflect the critical pressure (Ptrans) required to expand all aortic elastin fibers; at higher aortic...
pressures, collagen fibers and smooth muscle cells are recruited. Lanne et al.\textsuperscript{12,13} found that above \( P_{\text{trans}} \), the vessel is stiffer. They also found that the individual pressure-diameter curves show hysteresis. Those findings agree with the results of our study and are ascribed to the viscoelastic properties of the aorta. Both elastin and collagen contribute to wall mechanics; elastin is preferentially load-bearing at small distensions, and collagen is load-bearing at large distensions. Thus, the steep increase in diameter below the transition point mainly reflects the stretching of elastin, whereas both elastin and collagen contribute to the wall tension above the transition point.\textsuperscript{12,13} Thus, \( P_{\text{trans}} \) a functional index derived in vivo, provides useful anatomical and pathophysiological information on the aorta.

Indeed, the tensile modulus of an elastin fiber is \( \approx 750 \) mm Hg, which is relatively low for a connective tissue fiber.\textsuperscript{14,15} In contrast, collagen fibers are much stiffer. The tensile modulus of individual collagen fibers may be as high as \( 3.7 \times 10^6 \) mm Hg, which is 5000 times that of elastin.\textsuperscript{16} Experimental studies have indicated that vascular smooth muscle cells from several species all generate maximal stresses of 750 to 1500 mm Hg. The vascular smooth muscle cell contractile state is influenced by a variety of agents that may alter vascular stiffness.

We found that the aortic loop of normal subjects lies beneath the transition point in an area in which the blood pressure load is totally imposed on the elastin fibers of the aorta and a lot of pressure lag exists from peak systolic pressure to the transition point. In patients, the aortic loop operates near the transition point and, in some, the peak systolic blood pressure is higher than \( P_{\text{trans}} \). Under these circumstances, the elastin fibers are maximally extended and, over time, they degenerate.

Effects of Clinical Variables on the Aortic Line of Elasticity
The aortic line of elasticity was significantly related to age, history of hypertension, and hypercholesterolemia. These variables change the intrinsic elastic properties of the aorta independently of loading conditions.\textsuperscript{5,17,18} Furthermore, the interaction between age and hypertension suggested that the presence of hypertension in elderly patients has additional deleterious effects on the intrinsic properties of the aorta. Hypercholesterolemia has effects on the intrinsic aortic properties; these can be detected as alterations in the aortic line of elasticity; local atheromatous change does not necessarily occur. A similar finding was also reported in young subjects with familial hypercholesterolemia.\textsuperscript{19}

Response of Aortic Line to Vasodilating Drugs
Enalaprilat, despite blood pressure and diameter changes, did not change the intrinsic elastic properties of the aorta (passive mechanism). In contrast, 2 mechanisms are involved in diltiazem administration. One is a passive mechanism caused by a shift far away from the transition point. The other, an active mechanism, contributes as the aortic loop is shifted to a different sigmoid line of elasticity. This movement suggests active changes of the elastic properties of the aorta (change of the intrinsic elastic properties).

Importance of Aortic Line of Elasticity as a Predictor of Cardiovascular Events
The development of cardiovascular events can be predicted among patients with hypertension, coronary artery disease, and congestive heart failure on the basis of the aortic line of elasticity and the position of aortic loop on this line. This finding is consistent with the results of previous studies, which also concluded that a high pulse pressure or increased aortic stiffness are independent predictors of cardiovascular, and especially coronary, mortality.\textsuperscript{20-22} Our findings are also consistent with studies in which arterial alterations, as determined from the carotid elastic modulus, are strong independent predictors of cardiovascular mortality in patients with end-stage renal disease who are undergoing hemodialysis.\textsuperscript{23}

This study adds to those of previous investigators, first by demonstrating the relative prognostic power of the aortic curve of elasticity and second by demonstrating that the aortic line of elasticity can independently predict stroke, acute coronary events, and acute pulmonary edema in patients with hypertension, coronary artery disease, and heart failure. Specifically, we found that when \( b_1 \), \( b_3 \), and \( P_{\text{def}} \) increase, the risk of cardiovascular events will decrease because these predictors have a relative risk \(<1\) (Table 5). Thus, these parameters reflect beneficial aortic elastic properties.

Clinical Implications
The development of this new approach to analyze the pressure-diameter relation enabled us to distinguish between the intrinsic and extrinsic elastic properties of the aortic wall. As a consequence of this study, it is hoped that the understanding of the biologic functions of the aorta can be extended and that the behavior of the aorta can be explained and predicted with greater reliability. These results give insight into and explain the logic of therapies currently used for the treatment of hypertension, angina pectoris, and cardiac failure. They also show that therapeutic and prognostic benefits may be gained through a study of the intrinsic properties of the aorta.

Appendix
The goal of polynomial regression is to determine values for the parameters (\(A, B, C,\) and \(D\)) of the polynomial \( Y = A + Bx + Cx^2 + Dx^3\) that make the curve best fit the data points. The average deviation of the curve from the points is the square root of \( SS/df \), where \( df \) indicates degrees of freedom. This is also called the root mean square.\textsuperscript{11} The statistical significance is obtained by \( F = SS/S_2 \), where both numerator and denominator have \( NV \) degrees of freedom (\(N\) indicates the number of data points and \( V \), the number of parameters fit by the program).\textsuperscript{20}

To fit 2 sets of data to the same general model and to use the results to determine whether the 2 sets of data differ significantly, the following approach can be used.\textsuperscript{24} First, the 2 sets of data are analyzed separately. The overall values for the \( SS \) for the 2 sets of data analyzed separately are the sums of the individual values from each fit (\(SS_{\text{sep}} = SS_1 + SS_2\)). Similarly, the number of degrees of freedom (\( df \)) is the sum of the values from each fit (\( df_{\text{sep}} = df_1 + df_2 \)). Next, the 2 sets of data are pooled and analyzed simultaneously. This pooled fit yields values for \( SS_{\text{pool}} \) and \( df_{\text{pool}} \). The question is whether the separate fit is significantly better than the pooled fit. The significance of the improvement is determined from the \( F \) ratio, which is calculated as \( F = (SS_{\text{pool}} - SS_{\text{sep}})/(df_{\text{sep}} - df_{\text{pool}}) : (SS_{\text{sep}}/df_{\text{sep}}) \). To interpret the meaning of this \( F \) value, a statistical table is used to calculate the degrees of freedom.
convert it into a $P$ value. In using such a table, the numerator has $(df_{sep} - df_{pool})$ degrees of freedom, and the denominator has $df_{pool}$ degrees of freedom. A large $F$ value (with a corresponding low $P$ value) indicates that the separate fit is much better than the pooled fit, i.e., that the 2 sets of data are not well fit by 1 curve.

Acknowledgments

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References

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