Arterial Mechanical Properties in Dilated Cardiomyopathy

Aging and the Response to Nitroprusside

John D. Carroll, Sanjeev Shroff, Patricia Wirth, Mark Halsted, and Sol I. Rajfer

Departments of Internal Medicine, Section of Cardiology, and the Department of Pharmacological and Physiological Sciences, The University of Chicago, Chicago, Illinois 60637; and the Department of Electrical Engineering and Computer Science, The University of Illinois at Chicago, Chicago, Illinois 60637

Abstract

The effects of aging on arterial mechanical properties and the response to nitroprusside were examined in 25 patients with dilated cardiomyopathy. High-fidelity pressures were recorded with a multisensor catheter. Pulse wave velocity was determined between two sensors in the thoracic aorta. Arterial compliance was determined by an analysis of the diastolic waveform and cardiac output.

At baseline, despite a similar systemic vascular resistance, the pulsatile load (e.g., arterial compliance) and wave transmission characteristics (e.g., pulse wave velocity) were altered with aging. Arterial compliance was reduced in older (> 50 yr, $n = 8$) versus younger (< 35 yr, $n = 8$) patients (0.51±0.17 vs. 1.33±0.63 ml/mmHg, $P < 0.01$) and intermediate in those 35–50 yr of age ($n = 9$, 0.72±0.40 ml/mmHg). There was a positive correlation between age and pulse wave velocity ($r = +0.90$).

Nitroprusside infusion decreased resistance, increased arterial compliance, and lowered pulse wave velocity in all groups. Yet, advancing age was associated with a greater fall in wave velocity for a given fall in aortic pressure. The slope (K) of the relation between pulse wave velocity and aortic diastolic pressure progressively increased with age (0.01±0.03, 0.06±0.02, and 0.09±0.03 m/s-mmHg). Multiple linear regression analysis revealed a significant relation between K and age.

These data demonstrate that in older patients with dilated cardiomyopathy the left ventricle is coupled to an arterial circulation that has a greater pulsatile load, despite a similar steady load. Furthermore, these age-related changes in the arterial system affect the hemodynamic response to pharmacologically-induced vasodilatation. (*J. Clin. Invest.* 1991. 87:1002–1009.)

Key words: arterial properties • aging • cardiomyopathy • nitroprusside

Introduction

The loss of vascular elasticity with aging is well documented (1). Yet the presence of altered mechanical properties associated with aging is not well defined in patients with left ventricular dysfunction and overt congestive heart failure. This may be clinically important since the myopathic left ventricle is more sensitive to arterial load alterations and therapy is frequently directed at arterial load (2–4).

Left ventricular—arterial coupling concerns the relation between the heart as a pump and its connection to the hydraulic load presented by the arterial system. This arterial load can be divided into two components: a pulsatile load and a nonpulsatile load (5). The primary determinant of the nonpulsatile component of the arterial load is measured in the clinical setting as the systemic vascular resistance. A complete description of the arterial load, however, requires evaluation of the pulsatile component as well. The pulsatile component is measured as aortic input impedance and is modified by large artery compliance and pulse wave reflections (6). Several animal studies using an isolated heart preparation have established the importance of the pulsatile component of arterial load to left ventricular pump function (7, 8). Furthermore, the pulsatile wave propagation characteristics affect arterial reflections which, in turn, alter left ventricular afterload (9). Given that the myopathic heart is especially sensitive to changes in afterload, it is of interest to quantify arterial load more completely in patients with heart failure and to examine alterations in load that may be age related. Therefore, we examined both the pulsatile and nonpulsatile characteristics of arterial load in the cardiomyopathic state in different age groups.

Methods

Patient Characteristics

The research protocol was approved by The University of Chicago Clinical Investigation Committee and all patients gave written, informed consent. The research protocol was incorporated into their routine study.

The subject population consisted of 25 patients (6 women and 19 men) with the diagnosis of dilated cardiomyopathy. Their ages ranged from 16 to 71 yr and they were divided into three groups of patients according to age. The youngest were from 16 to 34 yr of age ($n = 8$); the middle group ranged in age from 35 to 50 yr ($n = 9$); and the oldest were from 51 to 71 yr of age ($n = 8$).

The majority of patients ($n = 22$) had idiopathic disease, two patients had a history of heavy alcohol use, and one had received adriamycin. Three had single coronary arterial diameter narrowing of > 50%, but none had clinical or angiographic evidence of a discrete infarction. Statistical analysis was completed both including and excluding these three patients. Those with obvious hypertensive heart disease were excluded. All had symptomatic congestive heart failure (New York Heart Association Functional Class II–IV). All had a moderately to severely dilated left ventricle with diffuse and marked hypokinesis on echocardiographic examination. The mean short axis end-diastolic dimension was 6.9 cm with a range of 5.3–8.6 cm, the mean end-systolic dimension was 6.0 cm with a range of 4.6–7.7 cm, and the mean fractional shortening was 14% with a range of 6–24%. Vasodilators were withheld at least 12 h before catheterization. Other medications were not administered the day of catheterization. 23 patients were

Address reprint requests to Dr. John D. Carroll, Hans Hecht Cardiac Catheterization Laboratory, The University of Chicago Hospitals, Box 124, 5841 S. Maryland Avenue, Chicago, IL 60637.

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chronically taking digoxin, 22 were taking furosemide, and 3 were taking other diuretics. Two patients (one in the young group and one in the old group) were receiving dobutamine at a low infusion rate (2 μg/kg per min) and it was discontinued 15 min before data acquisition.

Cardiac Catheterization

Patients received Diazepam (5 mg orally) before catheterization and Heparin (5,000 U, i.v.) when catheter insertion was complete. A thermodilution catheter was percutaneously placed via the femoral vein and advanced to the pulmonary artery. A multisensor, high-fidelity catheter (model #SSD-402; Millar Instruments, Houston, Texas) was inserted in the femoral artery and advanced to the left ventricle. A high-fidelity pressure sensor at the catheter tip recorded left ventricular pressure. A second sensor was located 5 cm distal, immediately above the aortic valve, and a third sensor was located in the descending thoracic aorta 25 cm distal to the aortic valve. The high-fidelity catheter was presoaked in saline for at least 30 min before insertion. Calibration was against a mercury reference. The fluid-filled side-port of the femoral arterial sheath connected to an external transducer (P230b; Gould Statham) was used to verify in vivo the calibration of the micromanometers. High-fidelity pressures from the three locations were digitized on-line or from magnetic tape at a sampling rate of 1,000 Hz and stored on diskette (IBM PC). At least 10 beats were averaged for the determination of standard variables including maximum left ventricular $+dP/dt$, left ventricular end-diastolic pressure, and aortic pressures. Left ventricular stroke work index ($LVSWI$) was calculated as:

$$LVSWI = SI^{*}(LV_{ej} - LV_{ed})^{*}0.0136$$

where SI is stroke volume index; LV_{ej}, mean left ventricular ejection pressure; and LV_{ed}, left ventricular end-diastolic pressure (10). Thermodilution cardiac outputs were obtained and three determinations with < 10% variability were averaged.

After baseline hemodynamic measurements were acquired, nitroprusside was administered intravenously beginning at a rate of 0.125 μg/kg per min and increasing every 3–5 min until 2.0 μg/kg per min was attained or peak systolic arterial pressure declined to 90 mmHg. Data were recorded at multiple doses of nitroprusside (Fig. 1). Nitroprusside was administered to 20 of the 25 patients participating in the study. The average maximum dose achieved was 0.9 μg/kg per min with a range of 0.375 to 2.0 μg/kg per min.

Data Analysis

Pulse wave velocity. Digitized (1 kHz) data were obtained from two high-fidelity pressure sensors located 25 cm apart in the thoracic aorta. To determine pulse wave velocity the onset of the wavefront was identified at two locations; the transit time was then determined and divided into the distance between the two sensors (11, 12). The minimum pressure at the foot of the upstroke was used by a computer program to identify the wavefront at both aortic locations. The program computed pulse wave velocity on a beat-by-beat basis and also reported the minimum pressure at the onset of each beat. This aortic diastolic pressure was used as an index of the distending pressure of the aorta which is known to affect pulse wave velocity (6).

A plot of pulse wave velocity versus aortic diastolic pressure was constructed for each patient receiving nitroprusside, each point representing a single beat. At least 20 beats with distinct diastolic aortic pressures in the range of 50–100 mmHg were analyzed (Fig. 2) including data points during both the control period and during nitroprusside. The slope (K) of the relation between aortic diastolic pressure and pulse wave velocity was computed by linear regression analysis.

Arterial compliance. As described by Liu et al. (13), arterial compliance was computed using the area under the diastolic waveform. This method assumes a two-element Windkessel model during diastole. The area (A_d) under the diastolic pressure waveform was computed from the maximum pressure after the dicrotic notch (P_s) to minimum pressure near end-diastolic (P_d). Estimated arterial compliance (C) was calculated for each patient by the formula:

$$C = A_d/R^{*}(P_s - P_d)$$

where R is the systemic vascular resistance calculated from cardiac output and mean aortic pressure.

Statistical Analysis

In all tables and throughout the text, data are reported in terms of mean and standard deviation. Figures show mean values with standard errors. Analysis of variance was used to compare variables between groups. When more than two groups were being examined, further pair-wise comparisons were made with unpaired t test, adjusting the significance level for multiple comparisons using Bonferroni bounds ($P < 0.05/k$, where k = number of comparisons). Comparisons within each cardiomyopathic group, both before and after the highest dose of nitroprusside, were made using analysis of variance with repeated measures and paired t test with the significance level adjusted for multiple comparisons.

Multiple linear regression was used to relate pulse wave velocity (PWV) to distending pressure (P_{dia}) and age. As illustrated in Fig. 2, there is a linear relationship between distending pressure and wave velocity for a given patient; however, this relationship changes with

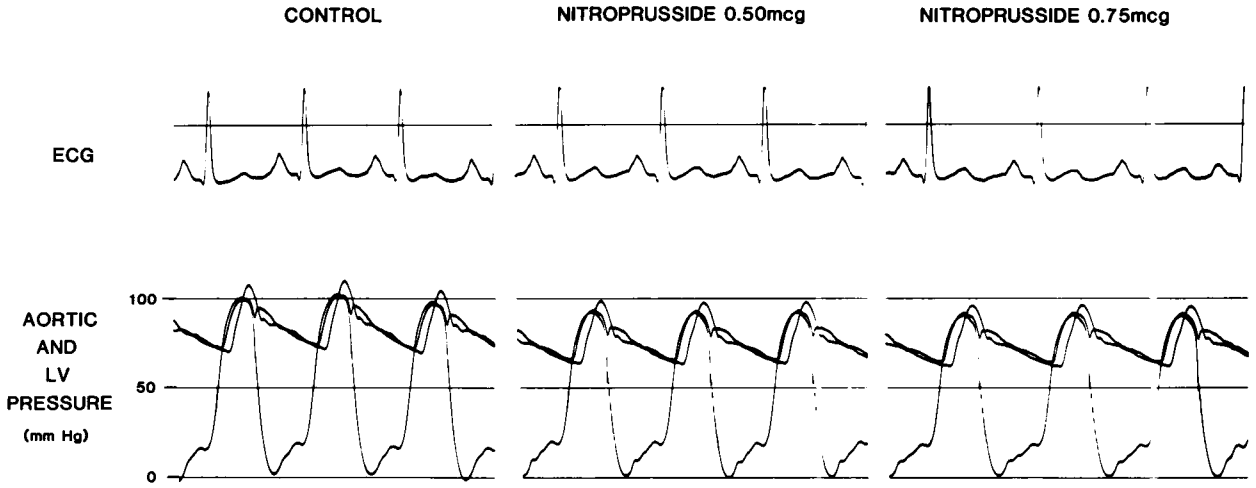

Figure 1. Raw data from a 33-yr old with dilated cardiomyopathy. High fidelity pressures from the left ventricle and two locations in the thoracic aorta were recorded with a multisensor catheter. Nitroprusside was infused to lower the distending pressure of the aorta and assess the effect on the mechanical properties of the arterial system.

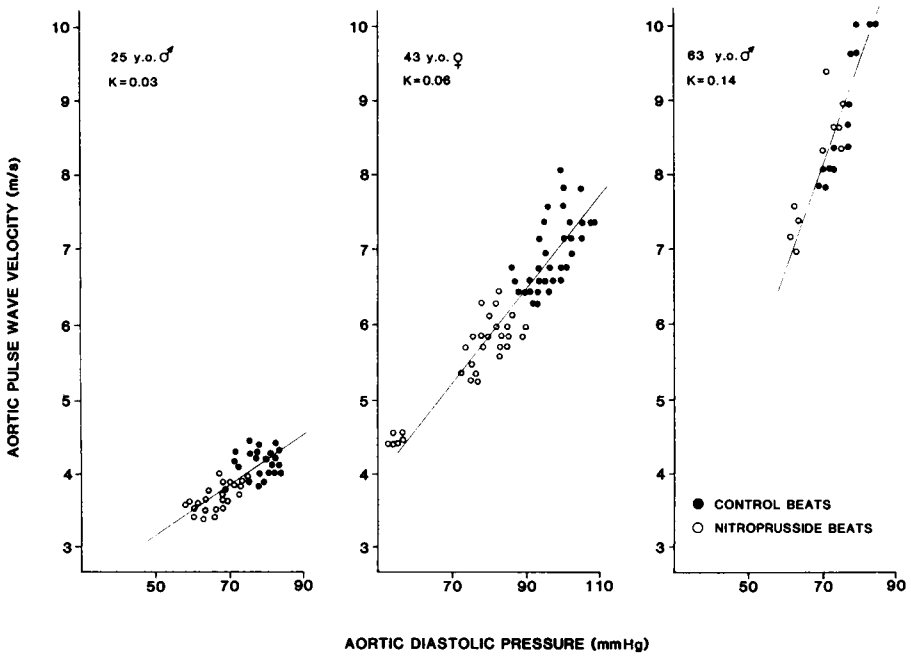

Figure 2. The relationship between pulse wave velocity and aortic diastolic pressure is shown for three patients of different ages but all with dilated cardiomyopathy. Note that as pressure was lowered by nitroprusside there was a fall in pulse wave velocity in all patients, but the relationship was much steeper (increased slope, K) for the oldest patient. This shows a differential response to vasodilator therapy.

age. Therefore, we subjected all data, i.e., from all patients and all levels of distending pressure (n = 1,973), to multiple linear regression analysis using the following model with four parameters (A_1–A_4):

$$PWV = (A_1 + A_2{*}\text{age})P_{dia} + (A_3{*}\text{age} + A_4).$$

The rationale for this model is that the slope and/or the intercept of the linear relation between PWV and P_{dia} can be modified by age and the dependence on age, as a first approximation, is also linear.

Patients with dilated cardiomyopathy were divided according to age into three groups of approximately equal size for statistical analysis. The three patients with coronary artery disease were all in the oldest group. Statistical analysis was completed both including and excluding these three patients.

Results

Baseline hemodynamic evaluation. Control values for the hemodynamic variables are presented in Tables I and II. Heart rate was similar in all groups as was cardiac index. Mean aortic pressure was significantly higher in the middle age group compared with the young age group, and in the older age group excluding the patients with coronary artery disease compared with the young age group. No other significant differences were present. Both left ventricular end-diastolic pressure and maximum positive dP/dt were similar in all groups.

Despite comparable values for stroke volume there was an increase in pulse pressure with aging (Table II). Furthermore, there was a progressive increase in pulse wave velocity with age (Fig. 3). The correlation coefficient relating baseline pulse wave velocity in the aorta to age was +0.90. For illustrative purposes, Fig. 3 also shows age and baseline pulse wave velocity data from nine patients found free of significant cardiovascular disease at cardiac catheterization.

Despite comparable values for systemic vascular resistance, arterial compliance progressively declined with age (Table II). This decline was significant for young versus middle and old groups (Table II).

Nitroprusside hemodynamics in all patients. Nitroprusside was infused in 20 patients (young group, n = 5; middle group, n = 9; old group, n = 6) to alter the distending pressure. Stroke volume increased from 40±18 to 53±23 ml ($P < 0.01$) and stroke work index increased from 20±10 to 27±11 g-m/M^2 ($P < 0.01$). The decrease in diastolic pressure from 82±12 to 71±11 mmHg ($P < 0.001$) was accompanied by a proportional reduction in pulse wave velocity (6.4±1.3 to 5.8±1.2 m/s, $P < 0.01$). Arterial compliance increased from 0.87±0.59 to 1.50±1.00 ml/mmHg ($P < 0.001$).

Aortic systolic pressure at the proximal measuring site decreased from 110±16 to 97±11 mmHg with nitroprusside ($P < 0.001$). Aortic systolic pressure at the distal site decreased from 115±19 to 99±14 mmHg ($P < 0.001$). The amplification of systolic pressure between the two sites was statistically significant ($P < 0.001$) at 5.0±3.8 mmHg during the control period, and was reduced to 1.5±3.6 mmHg during nitroprusside.

Nitroprusside hemodynamics in subgroups. The average maximum dose of nitroprusside achieved in each group was similar. Analysis of variance with repeated measures revealed a significant ($P < 0.0001$) decrease in systemic vascular resistance with nitroprusside in all three groups. In those < 35 yr systemic vascular resistance decreased with nitroprusside, from 1,822±834 to 1,441±676 dyn·s·cm^{-5}; in those 35–50 it decreased from 2,372±763 to 1,642±478; and in those > 50 it decreased from 2,328±877 to 1,637±449. However, there was no significant effect of age (P = 0.56) and nitroprusside–age interaction (P = 0.35). Thus, systemic vascular resistance was similar between groups both at baseline and after nitroprusside.

Similar analysis indicated that nitroprusside significantly (P = 0.0007) increased arterial compliance in all three groups. In those < 35 yr compliance increased from 1.55±0.71 to 2.41±1.04 ml/mmHg; and in those 35–50 yr it increased from 0.72±0.39 to 1.41±0.94 ml/mmHg; and in those > 50 it increased from 0.52±0.20 to 0.87±0.45 ml/mmHg. In contrast to systemic vascular resistance, there was a significant (P = 0.0083) effect of age. However, there was no nitroprusside–

Table I. Baseline Hemodynamic Data Obtained from Cardiomyopathic Patients

Patient group	Age	Heart rate	Cardiac index	Mean AOP	Maximum +d*P*/d*t*	LVEDP	Stroke work
	yr	*bpm*	*liter/min per M2*	*mmHg*	*mmHg/s*	*mmHg*	*g-m/m²*
Young (Y)							
Mean	26	91	2.24	81	1,011	22	19
SD	6	13	0.99	7	160	10	10
Middle (M)							
Mean	40	98	2.01	98	1,170	30	20
SD	3	12	0.82	7	159	9	10
Old (O)							
Mean	59	90	1.90	89	1,147	26	19
SD	7	10	0.36	13	374	8	10
Old* (O*)							
Mean	56	89	1.92	96	1,197	25	19
SD	7	8	0.37	12	397	8	13
All patients							
Mean	42	93	2.05	89.5	1,112	26	19
SD	15	12	0.75	11.5	248	9	10
P Values (after adjustment for multiple comparisons)							
Y vs. M	--	NS	NS	<0.01	NS	NS	NS
M vs. O	--	NS	NS	NS	NS	NS	NS
Y vs. O	--	NS	NS	NS	NS	NS	NS
M vs. O*	--	NS	NS	NS	NS	NS	NS
Y vs. O*	--	NS	NS	<0.05	NS	NS	NS

* Excludes patient with any coronary artery disease. bpm, beats per min; AOP, mean aortic pressure; +d*P*/d*t*, time derivative of left ventricular pressure; LVEDP, left ventricular end-diastolic pressure.

age interaction ($P = 0.25$) indicating that the effect of nitroprusside on arterial compliance was similar in all three groups and the baseline intergroup differences persisted after nitroprusside.

Pulse wave velocity and aortic diastolic pressure. The slope (K) of the relation between pulse wave velocity and aortic diastolic pressure was computed using data during nitroprusside infusion (Fig. 2). In those < 35 yr of age K averaged 0.01±0.03 m/s-mmHg, showing a minimal change in pulse wave velocity as pressure was altered. The middle group exhibited a K value of 0.06±0.02 ($P < 0.001$ vs. youngest). In the oldest group K averaged 0.09±0.03 ($P < 0.01$ vs. youngest), indicating that for a given change in distending pressure the oldest group had a greater change in pulse wave velocity.

Multiple linear regression analysis, relating pulse wave velocity to distending pressure (diastolic aortic pressure) and age revealed that only parameter A_3 was statistically not different from zero. The optimal values of parameters A_1, A_2, and A_4 were −0.0326±0.002 m/s-mmHg, 0.00149±0.00002 m/s-mmHg-yr, and 4.07 m/s, respectively. The multiple linear regression equation was ($r = 0.86$):

$$PWV = (0.00149*\text{Age} - 0.0326)P_{dia} + 4.07.$$

Multiple linear regression analysis done excluding the three patients with coronary artery disease revealed the equation ($r = 0.84$):

$$PWV = (0.00131*\text{Age} - 0.0168)P_{dia} + 3.35.$$

Thus, the slope of the PWV–P_{dia} relation increases with increasing age.

Discussion

Loss of arterial elasticity with aging is demonstrated in this study of patients with dilated cardiomyopathy. Three separate indices revealed this: an increase in pulse pressure for a given stroke volume, an elevated pulse wave velocity for a given distending pressure, and a reduction in compliance despite a similar systemic vascular resistance. Furthermore, the response to nitroprusside, in terms of the quantitative fall in pulse wave velocity for a reduction in aortic pressure, is shown to be influenced by the age. These findings indicate that the response to pharmacologic therapy in congestive heart failure can be influenced by age.

Age and arterial compliance. Studies by Avolio and coworkers have shown substantial increases in pulse wave veloc-

Table II. Arterial Mechanical Properties in Cardiomyopathic Patients

Patient group	Stroke volume	Pulse pressure	Pulse wave velocity	Systemic vascular resistance	Arterial compliance
	ml	*mmHg*	*m/s*	*dyn·s·cm^{-5}*	*ml/mmHg*
Young (Y)					
Mean	45	26	4.7	1,872	1.33
SD	24	8	0.4	789	0.63
Middle (M)					
Mean	38	30	6.5	2,373	0.72
SD	17	11	0.9	762	0.40
Old (O)					
Mean	38	37	7.9	2,206	0.51
SD	10	7	0.7	693	0.17
Old* (O*)					
Mean	35	39	7.6	2,440	0.44
SD	9	7	0.6	770	0.17
All patients					
Mean	40	31	6.4	2,159	0.85
SD	17	10	1.5	749	0.54
P Values (after adjustments for multiple comparisons)					
Y vs. M	NS	NS	<0.001	NS	<0.05
M vs. O	NS	NS	<0.01	NS	NS
Y vs. O	NS	<0.05	<0.001	NS	<0.05
M vs. O*	NS	NS	<0.05	NS	NS
Y vs. O*	NS	<0.05	<0.001	NS	<0.01

* Excludes patients with any coronary artery disease.

ity related to age in a large group of subjects free of overt cardiovascular disease (14, 15). Invasive data from Nichols et al. (16) have demonstrated that characteristic impedance derived from input impedance analysis rises with age indicating an increase in the pulsatile component of vascular load. Furthermore, O'Rourke and co-workers have reported age-related alterations in the systolic pulse contour that are presumably due to a loss of arterial compliance and an earlier return of reflections (17). In this study the effects of aging on pulse wave velocity and arterial compliance were documented, for the first time, in a group of patients with dilated cardiomyopathy, rather than in normal subjects. As depicted in Fig. 4, the alterations in wave velocity and pulse contour are visually apparent; suggesting a substantial aging effect.

Stroke volume and cardiac output have been shown by others to be slightly lower and systemic vascular resistance slightly higher in older versus younger, normal subjects (16). These variables were not age-related in our group of patients, presumably from the confounding influence of the cardiomyopathy increasing the range of these variables in each age group.

Determinants of arterial compliance. Factors other than age could influence the compliance of the arterial system. These factors include distending pressure, neurohumoral influences, geometric factors, and wall properties. Relatively small variations in distending pressure were present in our patients, especially when contrasted with the hypertensive patients studied by Liu and co-workers (18). Furthermore, in our study the pulse wave velocity and distending pressure relation was different between groups, which emphasizes that at identical distending pressures pulse wave velocity is still unique for patients of different ages.

The neurohumoral status of the patients reported in this study was not characterized although there is no reason to suspect that significant differences would exist between groups. All had an increase in resting heart rate indicative of the heightened sympathetic tone accompanying congestive heart failure.

The underlying structure of the arterial wall undergoes alterations with aging (1). The doubling of wave velocity between 20 and 60 yr of age in our patients would be produced by a fourfold increase in the elastic modulus of the arterial wall for a similar distending pressure (12).

Therefore, we feel that the differences in arterial mechanical properties seen in our patients were most likely due to age-related alterations in the arterial wall. Geometric changes may be additionally involved, but there was no evidence that dis-

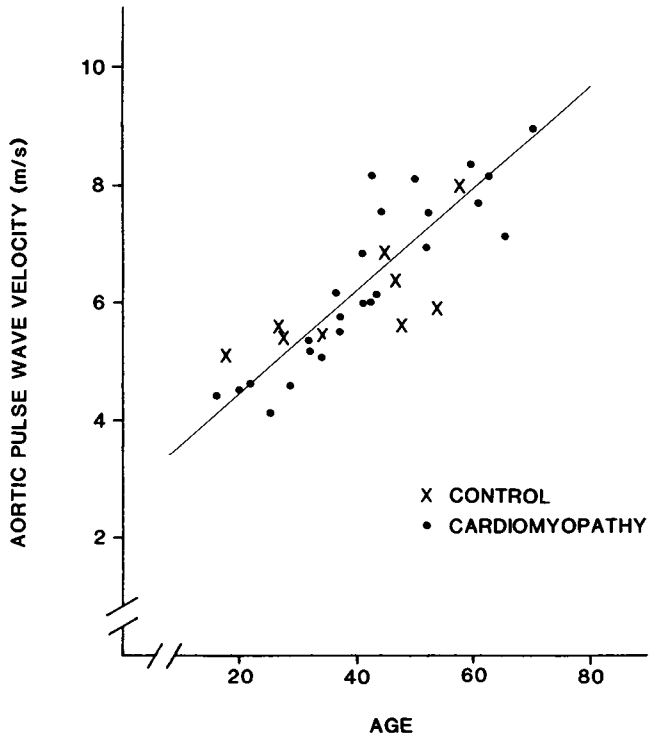

Figure 3. Data from all patients (n = 25) with dilated cardiomyopathy are shown in this plot of age and baseline pulse wave velocity. Pulse wave velocity increased with age. For illustrative purposes data from control patients (n = 9) free of significant cardiovascular disease are also included.

tending pressure and neurohumoral variations could account for our results.

Determinants of arterial load. A complete description of the arterial component of left ventricular load must include both the pulsatile and nonpulsatile components. Thus, quantitative information regarding arterial compliance and wave propagation characteristics, along with the nonpulsatile (characterized by systemic vascular resistance), are necessary to understand the interaction, or coupling, between the left ventricular and the systemic circulation.

This study has shown that one component of the pulsatile afterload, arterial compliance, is reduced in the elderly patient with heart failure. The associated increased wave velocity can alter reflections arising from impedance discontinuities and may represent yet another age-modified load to left ventricular shortening. Indeed, Laskey and Kussmaul have shown an early return of reflected waves in patients with heart failure (19). Pepine and colleagues have also shown increased reflection magnitude and reduced aortic compliance in heart failure (20).

In this study the pulsatile load was clearly increased in the older patients. The contribution of the increased pulsatile load to the depressed left ventricular performance cannot be quantified. Yet, one could hypothesize that the added burdens of ejection into a less compliant arterial system, and an early return of less attenuated reflected waves during systole in the older patient (Fig. 5) would further reduce the stroke volume of the myopathic ventricle.

The shape of the arterial waveform has been shown to be significantly affected by reflections that may return to the central aorta before or after aortic valve closure (21, 22). It has

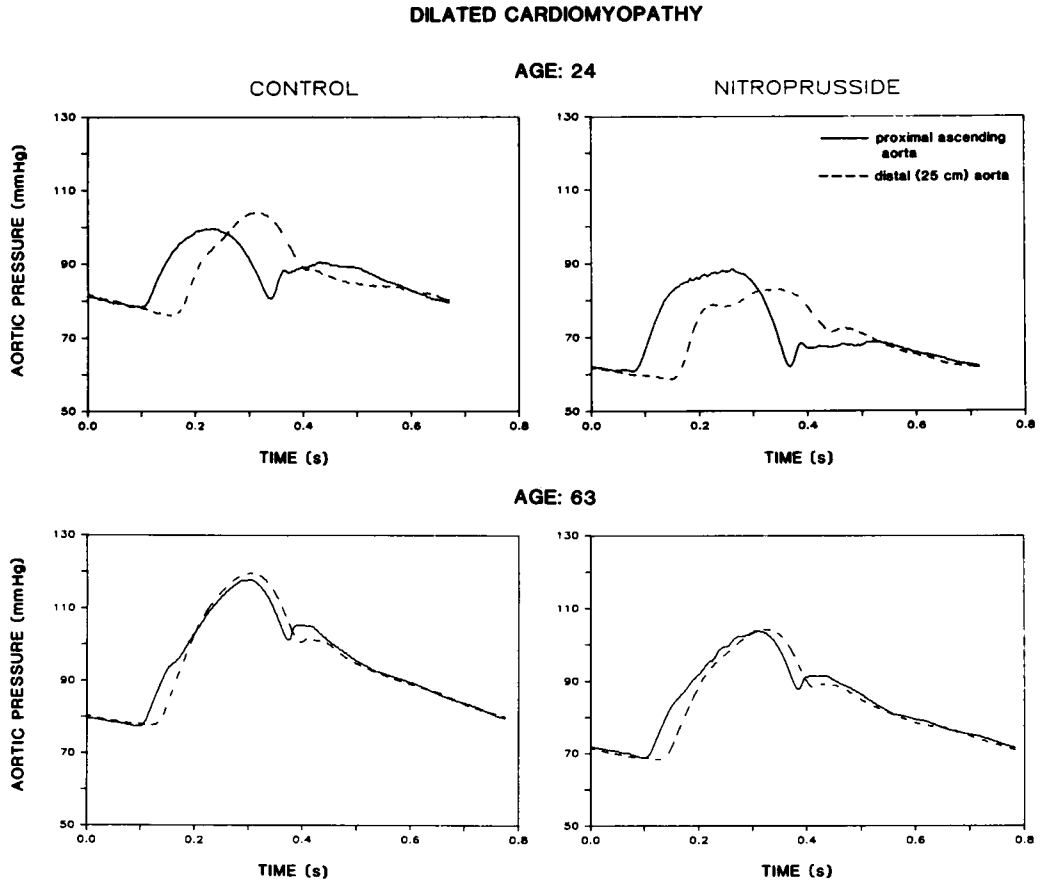

Figure 4. Data from two patients with dilated cardiomyopathy, one young and one old, are displayed before and during nitroprusside. Each panel contains two aortic pressure waveforms recorded from sensors 25 cm apart. In the control state the young patient had a lower pulse pressure and there was a clearly greater delay of the wavefront (i.e., slower wave velocity) between the two sensors as compared with the older patient. After nitroprusside this delay was increased for both patients and the diastolic pressure decay was modified. Note that the young patient had peak systolic pressure amplification at the distal sensor in the control state, but after nitroprusside had a fall in peak pressure with distal propagation of the wavefront.

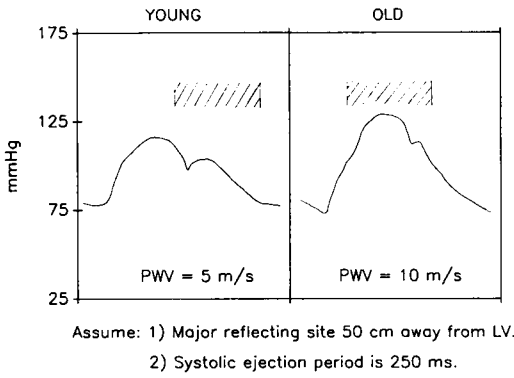

Figure 5. Schematic representations of the central aortic pressure waveform from a young (20-yr old) and old (70-yr old) patient are shown. The dashed area over each waveform represents the approximate time of reflections returning to the central aorta, assuming the location of major reflection sites and wave velocities. This results in pressure amplification in diastole in the young subject, but in systole for the older patient. This increased systolic pressure would be expected to modify ventricular ejection in a detrimental fashion especially in the presence of a cardiomyopathic ventricle. See text for details.

been suggested that there is a better match between the arterial system and the heart in the young individual since wave reflections return after aortic valve closure, thus augmenting pressure in diastole when coronary flow is maximum (17). As seen in Fig. 5 the range of wave velocities documented in this study are compatible with this interpretation. In the older individual it is clear that reflections return to the central aorta when the aortic valve is open, given our measured wave velocities and the approximate distance of major reflecting sites as reported by Murgo and co-workers (22).

Arterial load and cardiac failure. The detrimental combination of impaired pump function and increased vascular load has been appreciated in congestive heart failure and forms the basis for vasodilator therapy (4). Furthermore, it has been found that factors other than peripheral resistance also contribute to the arterial load in patients with congestive heart failure. Studies by Yin et al., Laskey et al., Merrillon et al., and Pepine et al. have examined aortic input impedance in congestive heart failure and have reported both normal and increased values of characteristic impedance (23–26). These divergent data may reflect differences in other determinants of arterial properties such as age which was not examined in any of these studies.

Nitroprusside. The arterial effects of nitroprusside have been studied by multiple investigators (23–27). The primary effect of reducing systemic vascular resistance appears related to its dilating effect at the arteriolar level. Other effects on aortic input impedance have suggested an effect on large artery function (23–27). This study documents the significant reduction in pulse wave velocity, increase in arterial compliance, and decrease in systemic vascular resistance after nitroprusside. This reduction in pulse wave velocity and increase in compliance should delay and attenuate reflections, as demonstrated by Laskey and Kussmaul (19). Furthermore, Brin and Yin have reported that nitroprusside reduces reflections in the absence of a significant reduction in characteristic impedance in patients with heart failure (27). Others have shown the effects of other vasodilators on reflections with pressure waveforms analysis (28, 29). This study is the first to quantify the alteration in wave propagation in the aorta that would mediate this delay in reflections in patients with congestive heart failure.

Age and response to nitroprusside. Systemic vascular resistance fell and compliance increased to a similar degree, in absolute terms, in the three groups of patients receiving nitroprusside. The net benefit of a given change in compliance on total arterial load, though, may be greater in older patients in whom the baseline value of compliance is markedly reduced. Yet, there does appear to be an age-related limit to the modification of arterial mechanical properties by nitroprusside since age-related intergroup differences in arterial compliance persisted after nitroprusside. Finally, the effect of nitroprusside on arterial compliance and wave velocity appears to be quantitatively dissimilar for patients of different ages (Fig. 6). For example, young patients had less modification of aortic pulse wave velocity than arterial compliance with nitroprusside infusion.

Distending pressure-pulse wave velocity relationship. In this investigation, the velocity of wave propagation is observed to be pressure dependent, previously only shown in animal studies (30). As seen in Fig. 2, it is possible to quantify the individual patient's pressure–pulse wave velocity relationship by the techniques developed in this project. This relationship provides a more complete description of the mechanical properties of any segment of the arterial tree than a single determination of pulse wave velocity. Patient to patient comparison of any measure of arterial elasticity is complicated by variability in distending pressure when recordings are made (18). This technique, therefore, allows distending pressure to be incorporated into the analysis.

The linearity of the distending pressure–pulse wave velocity relationship has also been documented in isolated canine carotid arteries (31). Furthermore, it was shown that the Moens-Korteweg equation, relating pulse wave velocity to the elastic modulus of the arterial wall at different degrees of distension, does quantitatively predict the relationship between pressure and pulse wave velocity (31).

Neurohumoral effects and nitroprusside. The relationship between pulse wave velocity and aortic diastolic pressure implies that the pulse wave velocity can be modified simply by a change in aortic distension. The presence of smooth muscle capable of shortening and/or generating force in response to

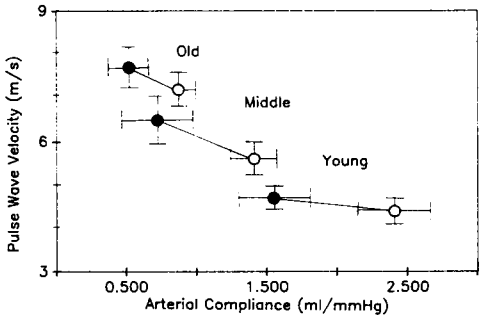

Figure 6. The relationship of pulse wave velocity and arterial compliance is shown for each age group both before (*closed circles*) and during nitroprusside (*open circles*) infusion. Pulse wave velocity of the thoracic aorta was modified less by nitroprusside than the global arterial compliance measurement, especially in the young patients. Both measurements of arterial mechanical properties, though, revealed an important relation to age.

neurohumoral factors and drugs may complicate the interrelation between the elastic modulus, vessel size, and distending pressure (12). Those receiving nitroprusside did not exhibit an increase in heart rate suggesting that baroreflexes were not activated as a result of the fall in blood pressure.

Summary. In conclusion, the results of this study demonstrate that the myopathic heart is coupled to an arterial circulation that progressively stiffens with age as indicated by increasing pulse wave velocity and pulse pressure and decreasing arterial compliance. Thus, at baseline, despite a similar systemic vascular resistance, the pulsatile load and wave transmission characteristics are different in older versus younger patients. These age-related changes in arterial mechanical properties influence the response to pharmacologically induced vasodilation and should be considered in the evaluation of vasoactive agents used to treat congestive heart failure.

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