Cardiac Consequences of Prolonged Exposure to an Isolated Increase in Aortic Stiffness

Isabelle Lartaud-Idjouadiene, Anne-Marie Lompré, Pascal Kieffer, Thérèse Colas, Jeffrey Atkinson

Abstract—In elderly patients, aortic stiffness is a major determinant of increased end-systolic stress leading to left ventricular (LV) hypertrophy with impaired cardiac performance. However, in a rat model of aortic elastocalcinosis (induced by vitamin D$_3$–nicotine [VDN] treatment), brief exposure (1 month) to increased aortic stiffness modified neither cardiac function nor cardiac structure. Here we report the impact of longer exposure (3 months) to aortic stiffness. Three months after induction of aortic stiffness, aortic characteristic impedance was measured in awake rats, 8 control and 10 VDN. Stroke volume was measured (electromagnetic probe) at baseline and after acute volume overload. LV weight/body weight ratio, collagen, and myosin heavy chain (MHC) contents were determined. Although aortic characteristic impedance increased (controls, 32±2; VDN rats, 50±8 10$^4$ dyne·s/cm$^2$; $P=0.0248$), stroke volume was maintained in VDN rats at baseline (controls, 223±18; VDN, 211±13 μL) and after volume overload (controls, 378±14; VDN, 338±15 μL). However, LV weight/body weight ratio (controls, 1.54±0.07; VDN, 1.73±0.05 g/kg; $P=0.0397$) and LV collagen content (controls, 31±4; VDN, 52±4 μg/g dry wt; $P=0.0192$) increased. A shift from $\alpha$-MHC (controls, 82±2%; VDN, 69±3%; $P=0.0056$) to $\beta$-MHC (controls, 18±2%; VDN, 31±3%; $P=0.0056$) was also observed. Three months’ exposure to increased aortic stiffness in VDN rats induced LV hypertrophy with moderate interstitial fibrosis and a shift in the MHC-isoform pattern. Such structural adaptation maintains LV performance.

(Hypertension. 1999;34:63-69.)

Key Words: heart failure ▪ ventricular fibrosis, left ▪ myosin ▪ hypertrophy, left ventricular ▪ cardiac afterload ▪ rats

In elderly patients, increased cardiac mass is linked to increased aortic stiffness.$^1$ With age, decreased aortic elasticity leads to increased aortic impedance and wave reflection velocity, which in turn lead to increased end-systolic stress, diminished cardiac performance, and left ventricular (LV) hypertrophy.$^2$ However, the increase in aortic impedance in humans is generally associated with increased mean pressure and therefore with increases in both the compliance and resistance components of cardiac afterload. The possibility that aortic stiffness alone could be a major determinant of increased end-systolic stress leading to cardiac dysfunction$^1$ is an attractive hypothesis in that it opens up new horizons in the treatment of cardiovascular pathologies related to aging, such as isolated systolic hypertension, in which mean arterial blood pressure is often normal.$^4$

However, experiments conducted to confirm this hypothesis in animal models or in the elderly have provided contradictory results. While some authors concluded that an acute decrease in aortic compliance leads to a decrease in cardiac performance,$^3$ others observed only minor changes in cardiac function.$^6$ Similarly, modest declines in resting stroke volume and cardiac output have been observed in some, but not all, elderly people following vascular stiffness associated or not associated with enhanced systemic resistance.$^8$ We therefore studied possible changes in cardiac performance in a rat model of chronically increased aortic stiffness with no change in peripheral resistance. Treatment with vitamin D$_3$ plus nicotine (VDN model) induces medial elastocalcinosis of the aorta with degradation of the retaining elastin network and an increase in aortic impedance and thoracoabdominal aortic pulse wave velocity, with no change in mean arterial blood pressure.$^9$–$^{11}$ In a first experiment,$^{14}$ we found no change in cardiac performance or mass after 1 month of exposure to increased aortic stiffness.

The aim of this second experiment was to evaluate the impact of a longer period of exposure to increased aortic stiffness on cardiac performance. After 3 months of exposure to increased aortic impedance, cardiac output was measured in awake, unrestrained rats at baseline and after acute volume overload. Aortic elasticity was evaluated from the measurement of aortic pulse wave velocity, aortic characteristic impedance, and elastic modulus.

To evaluate possible compensatory mechanisms maintaining cardiac performance, we first studied a possible decrease in venous capacitance. Our working hypothesis, based on observations in hypertensive patients,$^{15}$ was that were calci-
fication of the vena cava to occur in the VDN model, then venous capacitance would decrease, thereby increasing venous return and maintaining stroke volume in the face of increased aortic impedence. Second, we evaluated whether structural cardiac adaptation may explain the maintenance of cardiac performance by measuring LV weight/body weight ratio, collagen content, and the relative composition of the myosin heavy chain (MHC) isoforms. Our working hypothesis was that after an increase in aortic impedence, the myocardium becomes stiffer because of hypertrophy, interstitial fibrosis, and a shift in ventricular MHC from α- to β-MHC isoform. This allows stroke volume to be maintained despite the increased cardiac afterload.

Methods

Animals and VDN Treatment

Two-month-old (weight, 224±1 g; n=18) male outbread Wistar rats (WI/1co, IOPS AF/Han) were purchased from Iffa Credo (L’Arbresle, France) and housed under standard conditions (temperature, 21±1°C; humidity, 60±10%; lights, 6 AM to 6 PM). Rats were given food (UAR) and water ad libitum. All experiments were performed in conformity with the legislation of the European Union and Nancy University, Nancy, France.

One group of rats (VDN, n=10) was injected with vitamin D₃ (270 000 U/kg, 1 mL/kg IM; Dufrahral D, 1000, Dufahr B.V.) and received nicotine (25 mg/kg, 5 mL/kg PO; nicotine hydrogen tartrate; Sigma Chemical Company) at 9 AM. The nicotine administration was repeated at 6 PM on the same day. Controls (n=8) received 0.15 mol/L NaCl (intramuscularly) and distilled water (orally).

Cardiac Function and Aortic Stiffness:

Surgical Procedures

Three months after VDN treatment, an electromagnetic flow probe was implanted around the ascending aorta as previously described.14

Right thoracotomy (third intercostal space) was performed under sodium pentobarbital anesthesia (60 mg/kg IP) and positive-pressure ventilation (50 strokes/min, 10 mL/kg). A flow probe (2.7 mm; Skalar) was placed around the aorta 3 to 4 mm downstream from the aortic valve. The thorax was closed, and subatmospheric pressure (H₂O) was restored; the probe connector was guided subcutaneously to recover. The postoperative loss weight was similar (6±1%; n=18) in both groups.

After recovery, polyethylene cannulas (ID/OD, 0.58/0.96 mm; Merck-Biotrol) were introduced, under halothane (1%)/oxygen anesthesia, into the ascending aorta (through the left common carotid artery) and the abdominal aorta (through the right femoral artery) for measurement of central and peripheral aortic blood pressures. Venous cannulas (silicone elastomer, 0.63/1.19 mm; Sigma Medical) were introduced through the femoral veins into the thoracic vena cava for measurement of central venous pressure and into the abdominal vena cava for infusion. Cannulas were filled with heparinized (5 U/mL) 0.15 mol/L NaCl and passed subcutaneously to the back of the neck. Animals were allowed 24 hours to recover. The postoperative loss weight was similar (4±1%; n=18) in both groups.

Baseline Hemodynamics and Cardiac Response to an Acute Volume Overload in Awake Unrestrained Rats

Twenty-four hours after cannulation, conscious rats were connected to a sine wave electromagnetic flowmeter (MDL 1401; Skalar) and low-pressure transducers (Baxter). The signals were amplified, converted into digital form, and recorded online by a microcomputer at a sampling rate of 256 Hz (ie, 36 data points per beat at a heart rate of 420 bpm; see Results). After 30 minutes of equilibration, baseline values were determined beat to beat over periods of 4 seconds (28 heartbeats) and averaged; such recordings were performed every 30 seconds for 1 hour. For each group of 28 heartbeats, an algorithm detected the minimal (diastolic) and maximal (systolic) values of each pressure signal. The algorithm calculated mean aortic blood pressure from the waveform area, pulse pressure as the diastolic-systolic difference, and total peripheral resistance (mm Hg · min/mL) as central mean aortic blood pressure/mean cardiac output (see below). Transit times (ms) between central pressure signals were determined as previously described12,13 by an algorithm that systematically shifted in time the peripheral pressure waveform with respect to the central pressure waveform and determined the value of the time shift giving the highest correlation between the 2 pressure waveforms (coefficient of variability for repeated measurements < 2%).11–13 Pulse wave velocity (c/s) was calculated as the distance between the 2 cannula tips, measured after in situ fixation (see below) by sticking in situ a damp cotton thread onto the aorta.12,13

Aortic input impedence was evaluated from the central aortic pressure, and flow waveforms were averaged in the time domain and converted to Fourier series. Impedence modulus was calculated for each frequency as pressure modulus/flow modulus. Characteristic impedance (dyne · s/cm²) was obtained according to the method of Mitchell et al,16 which computes impedence values between the second and the 10th harmonic (ie, between 14 and 70 Hz at a fundamental frequency of 7 Hz; see Results). In the present study, characteristic impedence was calculated between 14 and 30 Hz because the dynamic frequency response of our pressure recording system is flat, with a phase lag <−6° up to 30 Hz and then slightly underdamped.12,13 The dynamic frequency response of the electromagnetic flow probe plus sine wave electromagnetic flowmeter was flat, with no phase lag up to 100 Hz (technical information from Skalar, Delft, Netherlands, with permission), therefore introducing no error into the calculation of characteristic impedence.

Mean central venous pressure (mm Hg), an index of cardiac preload, was calculated with the same program. Heart rate (bpm) was determined by counting the number of pressure cycles over a period of 4 seconds. Minimal and maximal values for cardiac output were measured, and mean cardiac output (mL/min) was calculated from the waveform area. Stroke volume (µL) was calculated as cardiac output/10^4/heart rate, and stroke work (mm Hg · mL) was calculated as stroke volume×10^3×(mean central aortic blood pressure−central venous pressure).

Systolic ejection time was determined as the time of the systolic increase in flow, and the cardiac flow cycle duration was determined as the time between 2 adjacent systolic peaks. Diastolic filling time was calculated as cardiac flow cycle duration−systolic ejection time. Diastolic filling time/cardiac flow cycle duration ratio was also determined.

Hemodynamics were also measured during acute volume overload induced by an intravenous injection in 1 minute of 40 mL/kg of phosphate-buffered saline at 37°C. Venous capacitance (mL/kg · mm Hg) was calculated as the reciprocal of the slope relating central venous pressure (mm Hg) to volume injected (mL/kg), according to Liard et al.17

During acute volume overload, cardiac output increased to a plateau of 45 seconds, whereas central venous pressure rose continuously. Cardiac output values were recorded during the last 10 seconds of the 1-minute infusion. The cardiac response to acute volume overload was used as an index of maximal cardiac performance, as proposed by Schoemaker et al.18

Aortic, Venous, and Cardiac Structure and Composition

At the end of the hemodynamic experiments, rats were killed by an overdose of sodium pentobarbital. After ligation of the ascending aorta, the heart was rapidly removed. Rats were perfused through the thoracic cannula for 30 minutes at their individual baseline central aortic mean blood pressures with 10% formaldehyde containing phosphate-buffered saline (NaCl 120 mmol/L, KCl 2.7 mmol/L, in a phosphate buffer 10 mmol/L, pH=7.4, at 25°C).
Aorta and abdominal vena cava were excised. A 5-mm sample of the descending thoracic aorta (Figure 1) was dehydrated in graded ethanol solutions and embedded in paraffin. Three 20-μm-thick sections were stained with hematoxylin-eosin for measurement of internal diameter and medial thickness (Saisam, Microvision Instruments).

Elastic modulus (EM) (10⁶ dyne/cm²) was calculated according to the Moens-Korteweg equation: 

\[ EM = \frac{PD_i}{h^2} \]

where \( P \) is aortic pressure, \( D_i \) is internal diameter, and \( h \) is medial thickness.

Wall stress (WS) (10⁶ dyne/cm²) was calculated from the Lamé equation: 

\[ WS = \frac{P D_i}{2 h} \]

where \( CAMBP \) (dyne/cm²) is central aortic mean blood pressure measured in awake unrestrained rat, \( D_i \) (cm) is internal diameter, and \( h \) (cm) is medial thickness.

A second 5-mm sample of the descending thoracic aorta (Figure 1) was removed for the determination of the wall content of the elastin-specific cross-linking amino acids desmosine and isodesmosine (μg/g aortic dry wt) by capillary zone electrophoresis and UV detection after hydrolysis in hydrochloric acid. Elastic modulus was greater (Table 1). VDN treatment produced a considerable fall in desmosine and isodesmosine content (controls, 7.9 ± 0.1 mm Hg; P = 0.0056) and the body weight (controls, 521 ± 17; VDN rats, 468 ± 15 g; P = 0.0348) were reduced in the VDN rats, suggesting that VDN treatment stunted growth. The thoracoabdominal length/body weight ratio (controls, 0.017 ± 0.001; VDN rats, 0.018 ± 0.001 cm/g; P = 0.6491) was similar in both groups. Aortic internal diameter and medial thickness were unchanged after VDN treatment (Table 1). Wall stress was not modified in VDN rats, but elastic modulus was greater (Table 1). VDN treatment produced a considerable fall in desmosine and isodesmosine content; there was an 18-fold increase in the calcium content of the descending thoracic aorta in VDN rats, and collagen content was unchanged (Table 1).

**Statistical Analysis**

Results are expressed as mean±SEM. For analysis of values obtained during acute volume overload, 2-way ANOVA was performed with group (control or VDN) and condition (baseline or overload) as variables. In all other cases, 1-way ANOVA was used. The null hypothesis was rejected at a probability level of 95% (P < 0.05). Comparisons of means were performed with the Bonferroni test.

**Results**

**Baseline Hemodynamics**

Treatment with VDN modified neither central mean aortic pressure nor total peripheral resistance (Table 1). Pulse pressure, aortic impedance and pulse wave velocity all increased in VDN rats (Table 1). Baseline central venous pressure was similar in both groups (controls, 2.6 ± 1.3; VDN rats, 2.2 ± 1.0 mm Hg; P = 0.7972), as were baseline cardiac output, stroke volume, stroke work, and heart rate (Table 2). Systolic ejection time was longer; the diastole/cycle ratio decreased (Table 2).

**Cardiovascular Response to Acute Volume Overload**

After volume overload, central venous pressure (controls, 17.7 ± 2.1; VDN rats, 20.0 ± 0.9 mm Hg; P = 0.2797) was similar in both groups, as was venous capacitance (controls, 3.1 ± 0.3; VDN rats, 2.9 ± 0.2 mL/kg · mm Hg; P = 0.5929). Cardiac output and stroke work increased in a similar way in both groups (Pgroup×condition > 0.05) because of a similar increase in stroke volume (Figure 2) with no change in heart rate. Two-way ANOVA, however, revealed a significant group effect for cardiac output, which was globally lower in VDN rats. Central mean aortic pressure did not change during volume overload in comparison to baseline and was similar in both groups (controls, 98 ± 4; VDN rats, 103 ± 6 mm Hg; P = 0.4924).

**Aortic, Venous, and Cardiac Structure and Composition**

The length of the thoracoabdominal aorta (controls, 8.8 ± 0.2; VDN rats, 7.9 ± 0.1 cm; P = 0.0056) and the body weight (controls, 521 ± 17; VDN rats, 468 ± 15 g; P = 0.0348) were reduced in the VDN rats, suggesting that VDN treatment stunted growth. The thoracoabdominal length/body weight ratio (controls, 0.017 ± 0.001; VDN rats, 0.018 ± 0.001 cm/g; P = 0.6491) was similar in both groups. Aortic internal diameter and medial thickness were unchanged after VDN treatment (Table 1). Wall stress was not modified in VDN rats, but elastic modulus was greater (Table 1). VDN treatment produced a considerable fall in desmosine and isodesmosine content; there was an 18-fold increase in the calcium content of the descending thoracic aorta in VDN rats, and collagen content was unchanged (Table 1).

The calcium content of the vena cava was unchanged (controls, 7 ± 2; VDN rats, 10 ± 2 μmol/g dry wt; P = 0.4530), whereas that of the LV wall was 4-fold higher in VDN rats (Table 2).

---

**Figure 1.** Left ventricle and aorta, showing the positions of the 2 cannula tips and the sites where samples were removed for the determination of LV composition, aortic geometry, and composition.
Heart and LV weight did not decrease in VDN rats (Table 2) despite evidence of failure to thrive (see above). The LV weight/body weight ratio was significantly higher in VDN rats (Table 2). LV collagen content was 2-fold higher in VDN rats (Table 2). The determination of the LV MHC-isoform profile revealed a significant decrease in α-MHC and an increase in β-MHC (Table 2).

**Discussion**

Despite 3-months’ exposure to an increased capacitive component of afterload, no change in the cardiac performance was noted. Stroke volume was not impaired in VDN rats, either under baseline conditions or after a volume overload. The lack of change in cardiac performance may be due to compensatory changes in structure. LV weight/body weight ratio increased, moderate LV fibrosis occurred, and there was a shift of the ventricular MHC-isoform pattern to the β-isoform. Simultaneously, systolic ejection time lengthened and the diastolic time/cycle time ratio decreased.

**A Normotensive Rat Model of Aortic Stiffness**

Treatment of young rats with VDN leads to calcium deposition on the medial elastic fibers near the lumen. Elastic fiber calcification leads to damage of the elastic network, as shown by a decrease in the aortic wall content of the elastin-specific cross-linking amino acids desmosine and isodesmosine. The fall in elastin is correlated to the increase in the calcium content. It is not associated with compensatory fibrosis, as has been suggested to occur with aging in humans. Aortic stiffness (as demonstrated by increases in aortic characteristic impedance, pulse wave velocity, and elastic modulus) occurred in the absence of any change in aortic mean pressure, geometry, or wall stress. This confirms previous results showing that the increase in aortic stiffness arises from a change in wall composition and that elastocalcinosi is the major factor inducing aortic stiffness in the VDN model.
Methodological Limitations

Before the cardiac consequences of aortic stiffness in the VDN model are discussed, several points should be highlighted concerning the methodology we used. We refer to an article by Mitchell et al. as the basis for the calculation of characteristic impedance. However, as we worked in awake animals, we used thin, fluid-filled catheters, with a limited frequency response (at 30 Hz, there is a 17% amplification and a 6° phase lag of the pressure signal) instead of transducer-tip catheters. This could contribute to distortion of the pressure curves and to overestimation of characteristic impedance \( (34.4 \pm 8.8) \times 10^3 \text{ dynes/cm}^2, n=88 \) observations in 3 anesthetized Wistar rats implanted with a polyethylene cannula, +50%, \( P<0.0001 \) versus \( 16.4 \pm 0.4 \times 10^3 \text{ dynes/cm}^2, n=84 \) observations in the same rats implanted with a Microtip SPR-407 transducer [Millar Instruments] at similar central mean aortic pressures [global mean, 121±2 mm Hg], cardiac output [70±2 mL·min⁻¹], and heart rate [401±2 bpm] for both conditions). It could be argued, however, that such distortion of the pressure curves occurs in a similar way in both control and VDN rats, and the comparison between the groups remains valid.

Second, Mitchell et al. used 10 harmonics to calculate characteristic impedance. Given the frequency limitations of our fluid-filled catheter, only 4 harmonics were used in the present study, leaving only 2 harmonics to assess the effects of reflected waves. However, we have previously shown that augmentation index and travel time of the reflected wave are unchanged in VDN rats, despite the lower body weight and shorter aortic path length in these animals. Therefore, we argue that the increased characteristic impedance observed in VDN rats results primarily from stiffening of the aortic wall.

The third point refers to the initial stunting of growth and toxicity problems due to VDN treatment. VDN rats lose weight during the first 8 days after treatment because they stop eating and drinking; some rats (<10%) may die from acute hypercalcemia-induced renal failure and cardiomyopathy. Then rats recover, with a growth rate and plasma composition similar to those of control rats, indicating that VDN rats are in good health but with a lower body weight.

Cardiac Performance

Despite the isolated increase in aortic stiffness, baseline stroke volume and cardiac output remained unchanged in VDN rats. The ventricular response to an acute increase in end-diastolic volume was globally unaffected in VDN rats as cardiac output, stroke volume, and stroke work increased in a similar way in both groups.

Several hypotheses could be proposed to explain why cardiac performance was maintained. First, according to Safar and London, stroke volume could be maintained in the presence of aortic stiffness by a decrease in venous capacitance followed by an increase in cardiac filling pressure. This is not the case in VDN rats, since venous capacitance remained normal. On the other hand, since blood volume expansion investigates the mechanical properties not only of the venous system but also of the left ventricle in diastole, a small reduction of venous capacitance is expected as a consequence of the increased myocardial stiffness due to moderate fibrosis. At this stage of adaptive hypertrophy, however, the increased stiffness of the left ventricle has not attained a degree that would modify volume distribution. The lack of vein calcification could also account for the lack of change in venous capacitance in VDN rats.

![Figure 2. Cardiac performance measured under baseline conditions and after acute volume overload (40 mL/kg of phosphate-buffered saline at 37°C in 1 minute) in controls (●, dotted lines) and VDN rats (●, solid lines). Results of the 2-way ANOVA were as follows, for \( P_{\text{group}}, P_{\text{condition}}, \) and \( P_{\text{group} \times \text{condition}} \) respectively: cardiac output (mL/min), 0.0350, <0.0001, and 0.2217; stroke volume (µL), 0.1044, <0.0001, 0.3592; stroke work (mm Hg·mL), 0.7299, 0.0045, 0.5136; and heart rate (bpm), 0.4238, 0.3634, 0.9879.](http://hyper.ahajournals.org/ Downloaded from)
The second explanation for a lack of change in cardiac performance is based on intrinsic structural adaptation. In the present study, heart and LV weight did not decrease in VDN rats despite evidence of failure to thrive, revealing ventricular hypertrophy, which could be one element maintaining cardiac performance. Such hypertrophy may reflect myocyte and/or nonmyocyte cell growth. Because we did not measure myocyte cell size in our model, we cannot conclude whether myocyte cell growth participates in the LV hypertrophy. The moderate increase in ventricular collagen content suggests remodeling of the myocardial interstitium, leading to increased systolic and diastolic myocardial stiffness. At this stage of adaptive hypertrophy, the accumulation of interstitial collagen reduces the dissipation of myocyte-generated force and thereby preserves stroke volume by increasing myocardial contractility. Thus, moderate interstitial fibrosis leads to diastolic LV dysfunction with a normal systolic function. Our results are in concordance with this hypothesis. Systolic ejection function is maintained, and the reduction of the ratio of diastole to cycle time, mainly related to the stiffening of the myocardium, is in favor of dysfunction of LV diastolic filling. On the other hand, the obligatory increase in systolic ejection period produced by a stiffened arterial tree and a shift of the ventricular MHC-isomorph pattern from α-MHC to β-MHC requires that diastole shortens.

LV hypertrophy was associated with a shift of the ventricular MHC-isomorph pattern from α-MHC to β-MHC. The latter form develops a slower, more energy-efficient form of contraction. This shift prolongs systolic ejection time and may explain the maintenance of ventricular contractile properties in VDN rats. Such a shift from α- to β-MHC has been observed in experimental models of aging or hypertension in which adaptation of LV contraction is required to withstand the increase in hemodynamic stress. It should be noted that a direct effect of hypervitaminosis D on the α- to β-MHC shift is unlikely since vitamin D does not alter myosin isoform distribution in primary cultures of ventricular myocytes.

On the basis of our results, we suggest that after 3 months of exposure to an isolated increase in aortic stiffness, VDN rats are in an intermediate stage of compensated cardiomyopathy. However, the significant group effect observed for cardiac output during volume overload may be the first indication of a negative evolution in VDN rats, suggesting that longer exposure to increased aortic stiffness may lead to heart failure (with a fall in cardiac performance, a reduction in ejection fraction and stroke volume, a shortened ejection time, and more extensive myocardial fibrosis secondary to myocyte necrosis). At this stage, an interesting evaluation of the impact of arterial stiffness would be to study cardiovascular mortality of rats and relate it to systolic aortic blood pressure level, indices of aortic stiffness, or cardiac weight. No conclusion can be drawn until we perform such a long-term study. Preliminary results indicate that the exposure to aortic stiffness should be at least longer than 1 year; VDN rats do not seem to suffer from increased systolic arterial blood pressure or arterial stiffness and do not start to die earlier than control rats, up to 14 months of age (Lartaud-Idjouadiene, unpublished data, 1997).

In conclusion, 3 months’ exposure to increased aortic stiffness induced by elastocalcinosis did not modify cardiac performance. However, increased aortic impedance induced myocardial remodeling with an increase in LV weight/body weight ratio, moderate interstitial fibrosis, and a greater proportion of β-MHC. Such intrinsic cardiac adaptation may explain the maintenance of LV performance in VDN rats at an intermediate stage of compensated cardiomyopathy.

Acknowledgments
This study was supported by grants from the French Education and Research Ministry (Paris, France); the Regional Development Committee (Metz, France); the Greater Nancy Urban Council (Nancy, France); and the Henri Poincaré University (Nancy, France). The authors thank Chantal Jamnot, CNRS EP 1088 (Orsay, France), for isomyosin quantification and René Peslin, Claude Duvivier, INSERM U14 (Nancy, France), and Philippe Giûmelly, Laboratoire de Pharmacologie Cardiovasculaire, Faculté de Pharmacie (Nancy, France), for help with signal analysis. The Nancy group is part of the European Biomed network “EureCa.”

References
Cardiac Consequences of Prolonged Exposure to an Isolated Increase in Aortic Stiffness
Isabelle Lartaud-Idjouadiene, Anne-Marie Lompré, Pascal Kieffer, Thérèse Colas and Jeffrey Atkinson

Hypertension. 1999;34:63-69
doi: 10.1161/01.HYP.34.1.63

Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1999 American Heart Association, Inc. All rights reserved.
Print ISSN: 0194-911X. Online ISSN: 1524-4563

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://hyper.ahajournals.org/content/34/1/63

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Hypertension can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Hypertension is online at:
http://hyper.ahajournals.org//subscriptions/