Impact of arterial elastance as a measure of vascular load on left ventricular geometry in hypertension

Impact of arterial elastance as a measure of vascular load on left ventricular geometry in hypertension

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Objective **Effective arterial elastance (E_a), integrating the pulsatile component of left ventricular (LV) afterload, is an estimate of aortic input impedance. We evaluated relationships of E_a with left ventricular anatomy and function in essential hypertension.**

Design **A cross-sectional analysis in 81 normotensive and 174 untreated hypertensive individuals enrolled in a referral hypertension centre.**

Methods **Using echocardiography we determined left ventricular mass index (LVMI), relative wall thickness (RWT), stroke volume (SV), endocardial (FS_e) and midwall (FS_m) fractional shortening and total peripheral resistance (TPR). Carotid pressure waveforms were obtained by arterial tonometry, and end-systolic pressure (P_{es}) was measured at the dicrotic notch. E_a index (E_aI) was calculated as P_{es}/(SV index); LV elastance (E_{es}) was estimated as P_{es}/LV end-systolic volume, and ventriculo–arterial coupling was evaluated by the E_a/E_{es} ratio.**

Results **E_aI was higher in hypertensives than in normotensives (3.02 ± 0.63 versus 2.40 ± 0.52 mmHg/l per m^2; $P < 0.0001$). Using the 95% upper confidence limit in normotensives, hypertensives were divided in two groups with normal or elevated E_aI. The 38 hypertensives with elevated E_aI had higher RWT (0.41 ± 0.06 versus 0.37 ± 0.05), lower LVMI (87.5 ± 18.5 versus 96.8 ± 19.3 g/m^2), higher TPR (2247 ± 408 versus 1658 ± 371 dynes/cm s^{-5}) and lower FS_e and FS_m (35 ± 5 versus 39 ± 5 and 16 ± 2 versus 18 ± 2%; all $P < 0.05$) than patients with normal E_aI. E_a/E_{es} ratio was increased and cardiac output was reduced in hypertensives with elevated E_aI.**

Conclusions **High values of E_aI identify a minority of hypertensive patients characterized by elevated TPR, left ventricular concentric remodelling, depressed left ventricular systolic function and impaired ventriculo–arterial coupling. *J Hypertens* 1999, 17:1007–1015**

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Keywords: left ventricular afterload, arterial elastance, left ventricular hypertrophy, ventricular–vascular coupling, echocardiography, applanation tonometry, left ventricular function

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Introduction

It is known that the increased afterload in systemic hypertension may induce adaptive changes of left ventricular anatomy. Previous studies have demonstrated that the pattern of left ventricular adaptation in hypertension is polymorphic [1], reflecting the interplay of hemodynamic pressure and volume load [2,3]. Moreover, concentric left ventricular geometry has been reported to be associated with increased pulse wave velocity in hypertension [4].

The vascular component of left ventricular afterload is usually assessed in terms of mean blood pressure or total peripheral resistance. However, these measurements do not take into account the pulsatile characteristics of blood flow in arteries [5,6]. Effective arterial elastance (E_a), i.e. the ratio between end-systolic pressure and stroke volume, has been proposed as a measure of arterial load that integrates peripheral resistance, total vascular compliance, characteristic impedance and systolic and diastolic time intervals [7,8]. According to a recent study showing that effective arterial elastance provides a reliable estimate of aortic impedance [7], effective arterial elastance could be considered an appropriate index of the vascular load acting on the left ventricle in conditions such as hypertension or ageing in which the pulsatile component of the arterial load may be enhanced. Since it shares the same dimensional units as left ventricular elastance (E_{es}), effective arterial elastance has also been used to

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assess the ventricular–vascular coupling by means of the ratio E_a/E_{es} [8,9]. Previous studies demonstrate that maximal left ventricular stroke work is achieved when the ratio E_a/E_{es} is near unity, while maximal efficiency occurs when E_a/E_{es} ratio approximates 0.5 [10,11].

This study was undertaken to investigate the influence of vascular afterload, as measured by effective arterial elastance, on left ventricular geometry and systolic function in uncomplicated essential hypertension.

Methods

Study population

The study was conducted in 81 apparently healthy normotensive individuals and 174 essential hypertensive patients, aged 25–88 years. Hypertension was defined as clinic systolic blood pressure $\geqslant 140$ and/or diastolic blood pressure $\geqslant 90$ mmHg in two or three measurements taken by mercury manometer at 1-week intervals. Individuals with signs or symptoms of coronary artery disease, heart failure or valvular heart disease were excluded. None of the patients had left ventricular wall motion abnormalities on echocardiogram. One-hundred and seven (61.5%) hypertensive individuals had been previously taking antihypertensive medications that were discontinued at least 3 weeks before the study, while the remaining 67 patients were never treated. Body habitus was evaluated by body mass index (BMI) (kg/m^2 of height) and body surface area (obtained from body height and weight by standard nomograms).

The study protocol had been approved by the Committee on Human Rights in Research of Cornell University Medical College in 1989 and at intervals thereafter.

Echocardiography

Two-dimensionally guided M-mode tracings were used to obtain left ventricular dimensions according to the recommendations of the American Society of Echocardiography [12,13]. Measurements were performed on several cycles using a digitizing tablet and averaged. Left ventricular mass was calculated according to the Penn Convention [14,15] and adjusted for body surface area. To take into account the impact of obesity (72 individuals had BMI $> 28\ kg/m^2$), left ventricular mass was also adjusted for body height to the power of 2.7 [16]. Left ventricular relative wall thickness was calculated as $2 \times$ posterior wall thickness/end-diastolic internal dimension. Patterns of left ventricular geometry in hypertensives were defined as previously described [1]; patients were classified as abnormal if the left ventricular mass index exceeded $108\ g/m^2$ in women or $118\ g/m^2$ in (men) [17] or the relative wall thickness exceeded the 95% upper confidence limit of the age-predicted value (from 0.42–0.48 according to the age decade) [18]. Stroke volume was calculated from end-systolic and end-diastolic left ventricular volumes, using the Teichholz formula [19]; in a subgroup of 51 normotensive and 42 hypertensive individuals stroke volume was additionally calculated from the Doppler time-velocity integral of trans-aortic valvular flow and aortic valve area [20]. Total peripheral resistance was calculated as (mean blood pressure $\times$ 80)/cardiac output. Meridional end-systolic stress was calculated as previously reported [1]; in addition, circumferential end-systolic stress was calculated by the method of Gaasch and coworkers [21]. Left ventricular ejection performance was assessed by both endocardial and midwall [22] fractional shortening and expressed as percentage of the value predicted from the relations of endocardial fractional shortening to meridional end-systolic stress and of midwall fractional shortening to circumferential end-systolic stress obtained in a sample of 430 normotensive individuals [18]. These variables were called stress-corrected endocardial and midwall shortening.

The ratio between M-mode derived stroke volume and carotid pulse pressure (SV/PP) was calculated as an estimate of total arterial compliance [23,24].

Pulse wave recording, augmentation index and effective arterial elastance

Pressure waveforms of the common carotid artery were obtained as described elsewhere [25–27], using high-fidelity applanation tonometry [28]. After external calibration by brachial sphygmomanometric mean blood pressure, a dedicated mouse-driven software written by an investigator (R.P.) allowed measurement of actual carotid blood pressures, which closely reflect the pressure values in the ascending aorta [29]. After identifying in the carotid pressure waveform the inflection point (P_i) due to the return of reflected pressure waves, the augmentation index was calculated as percentage of [(carotid peak systolic pressure – P_i)/carotid pulse pressure] [30] to estimate the impact of pressure wave reflection on central hemodynamics. Effective arterial elastance was calculated as the ratio of end-systolic pressure (estimated at the carotid dicrotic notch) to stroke volume [8]. Since stroke volume is related to body size, effective arterial elastance was also calculated after indexation of stroke volume to body surface area (E_aI) [31].

Left ventricular end-systolic elastance was calculated from the ratio of end-systolic pressure (at carotid dicrotic notch) to left ventricular end-systolic volume (E_{es}) [32]. Left ventricular–arterial coupling was evaluated by the ratio E_a/E_{es} [8,33,34].

Statistical analyses

Data were stored and analysed by the Crunch[4] Statistical Package (Crunch Software Corporation, Oakland,

California, USA). Relations between continuous variables were evaluated by Pearson's least squares method. Independent predictors of endocardial and mid-wall fractional shortening were evaluated by stepwise forward multiple regression analyses. The Student's *t* test was used to compare normotensive and hypertensive individuals and hypertensive patients with normal and high E_aI. One-way ANOVA followed by Dunnett's post-hoc test was performed to compare hypertensive individuals with high or normal E_aI with normotensive control individuals. Comparisons among frequencies were performed by Chi-square statistics. Data are expressed as mean ± SD. A two-tailed *P*-value less than 0.05 was considered to be statistically significant.

Results

Characteristics of normotensive and hypertensive individuals

Demographic characteristics of normotensive and hypertensive individuals are summarized in Table 1. Hypertensive patients were significantly older and had higher BMI, heart rate and augmentation index than normotensive control individuals. Left ventricular wall thicknesses, mass index and relative wall thickness were significantly larger in hypertensive than in normotensive individuals (Table 2), while stroke index was similar between the two groups. In the subgroup of 93 individuals in whom Doppler-derived stroke volume was available, M-mode and Doppler determinations were similar (average values 80.1 ± 18.1 versus 78.3 ± 18.2 ml, respectively; $P = 0.33$) and significantly related ($r = 0.55$; $P < 0.01$), in agreement with previous reports [35–36]. The Bland and Altman diagram [37] showed no systematic errors in the estimation of stroke volume by M-mode method (Fig. 1). As a consequence, M-mode and Doppler-derived E_a were similar (1.42 ± 0.41 versus 1.45 ± 0.41 mmHg/l; $P = 0.34$) and strongly related to each other ($r = 0.71$; $P < 0.0001$).

Table 1 **Demographic and hemodynamic characteristics of normotensive and hypertensive individuals**

	Normotensive individuals	Hypertensive patients
Number	81	174
Age (years)	50 ± 17	56 ± 12**
Sex (m/f)	54/27	108/66
Body mass index (kg/m^2)	25.0 ± 4.0	26.7 ± 4.0**
Body surface area (m^2)	1.84 ± 0.23	1.89 ± 0.23
Brachial systolic blood pressure (mmHg)	123 ± 12	159 ± 20†
Brachial diastolic blood pressure (mmHg)	72 ± 9	95 ± 11†
Heart rate (beats/min)	64 ± 9	68 ± 11**
Augmentation index (%)	6 ± 14	18 ± 11**

Data are means ± SD. ** $P < 0.01$. † $P < 0.01$, by design.

Cardiac index, total peripheral resistance and end-systolic stress were significantly higher in hypertensive than in normotensive individuals. The stroke volume to pulse pressure ratio was significantly reduced in hypertensive individuals. Stress-corrected endocardial fractional shortening was significantly higher and midwall shortening lower in hypertensive than in normotensive individuals. E_a, E_a index and E_{es} were higher in hypertensive individuals, while the ratio E_a/E_{es} was not different in normotensive and hypertensive individuals and closely approximated the value of 0.5 at which ventricular efficiency is considered to be maximal [10,11].

Relations of effective arterial elastance with left ventricular structure and function

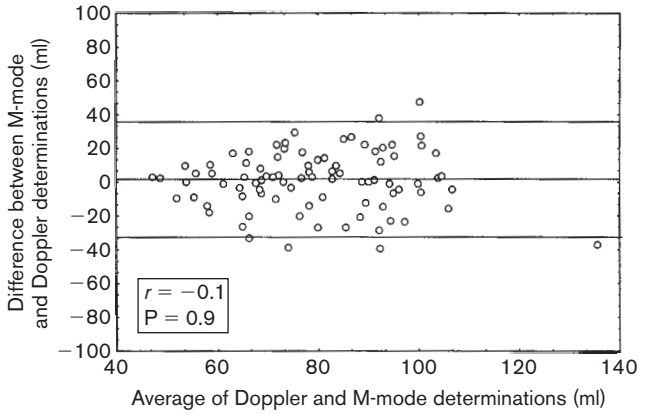
Left ventricular relative wall thickness, endocardial and midwall fractional shortening were significantly related

Table 2 **Left ventricular anatomy, function and effective arterial elastance in normotensive and hypertensive individuals**

	Normotensive individuals	Hypertensive patients
Left ventricular diastolic posterior wall thickness (cm)	0.81 ± 0.13	0.95 ± 0.12**
Inter-ventricular diastolic septal thickness (cm)	0.85 ± 0.14	1.00 ± 0.14**
Left ventricular diastolic diameter (cm)	4.94 ± 0.49	5.03 ± 0.51
Left ventricular mass/height$^{2.7}$ (g/m$^{2.7}$)	34 ± 8	43 ± 9**
Left ventricular relative wall thickness	0.33 ± 0.06	0.38 ± 0.06**
Stroke index (M-mode) (ml/m^2)	41.8 ± 7.0	43.4 ± 8.6
Stroke index (Doppler) (ml/m^2) ($n = 51$ and 42)	41.1 ± 7.1	42.5 ± 8.5
Cardiac index (l/min/m^2)	2.6 ± 0.5	2.9 ± 0.7**
Total peripheral resistance (dynes/cm sec^{-5})	1549 ± 420	1786 ± 450**
Stroke volume/carotid pulse pressure (ml/mmHg)	1.86 ± 0.81	1.63 ± 0.70*
Meridional end-systolic stress (kdynes/cm^2)	64 ± 14	73 ± 21**
Circumferential end-systolic stress (kdynes/cm^2)	173 ± 32	201 ± 52**
Endocardial fractional shortening (% of predicted)	102 ± 10	109 ± 12**
Midwall fractional shortening (% of predicted)	104 ± 13	100 ± 12*
E_a (mmHg/ml)	1.3 ± 0.4	1.6 ± 0.4**
E_a index (mmHg/ml/m^2)	2.40 ± 0.52	3.02 ± 0.63**
E_{es} (mmHg/ml)	2.8 ± 1.1	3.6 ± 1.5**
E_a/E_{es}	0.51 ± 0.16	0.50 ± 0.18

Data are means ± SD. Effective arterial elastance; E_{es}, left ventricular end-systolic elastance (single-point estimate).
* $P < 0.05$, ** $P < 0.01$. E_a.

Fig. 1



Bland and Altman diagram on Doppler and M-mode determination of stroke volume. Mean difference between the two determinations was 1.8 ml (solid line). The dotted lines indicate 2 standard deviations above and below the mean difference. Difference between measurements was not related to the average value, indicating the absence of systematic errors due to the magnitude of the parameter.

to E_aI both in normotensive and hypertensive individuals (Table 3). These relations were closer than the relations of these parameters with systolic, diastolic and carotid end-systolic blood pressures. Posterior wall thickness was also significantly related to E_aI, although it showed the closest relations with carotid end-systolic pressure in normotensives and with brachial diastolic blood pressure in hypertensives (Table 3). Negative relationships were found between left ventricular mass and E_aI, that attained statistical significance in hypertensive individuals.

Left ventricular posterior wall thickness ($r = 0.35$; $P < 0.01$), relative wall thickness ($r = 0.36$; $P < 0.01$) and mid-wall fractional shortening ($r = -0.36$; $P < 0.01$) were significantly related to Doppler-derived E_aI in the subset of individuals in whom Doppler-derived stroke index was available.

In hypertensive patients, both endocardial and midwall fractional shortening, expressed as a percentage of the predicted value, were inversely related ($r = -0.62$ and $r = -0.50$, respectively; both $P < 0.0001$) to the E_a/E_{es} ratio (Fig. 2).

Demographic and echocardiographic characteristics in hypertensive individuals with normal or elevated effective arterial elastance

The upper normal 95% confidence limit of effective arterial elastance index was calculated in normotensive individuals and used to identify hypertensive patients with normal ($E_aI \leq 3.43$ mmHg/l per m^2) or increased ($E_aI > 3.43$ mmHg/l per m^2) effective arterial elastance index. E_aI was increased in 38 hypertensive individuals (21.8%) and normal in 136 (3.9 ± 0.4 versus 2.8 ± 0.4 mmHg/l per m^2, respectively). Patients with normal or increased effective arterial elastance did not differ in age, gender distribution, BMI, heart rate or brachial systolic and pulse pressures. Elevated E_aI was associated with higher brachial diastolic blood pressure and carotid peak systolic and end-diastolic blood pressures; as partially expected as consequence of group definitions, carotid end-systolic pressure and body surface area were greater in hypertensives with elevated E_aI (Table 4). Augmentation index was similarly elevated in the two hypertensive groups compared to normotensives (Table 4), and it was positively related to both carotid end-systolic pressure ($r = 0.38$; $P < 0.001$) and E_a ($r = 0.21$; $P < 0.001$) in the whole hypertensive population.

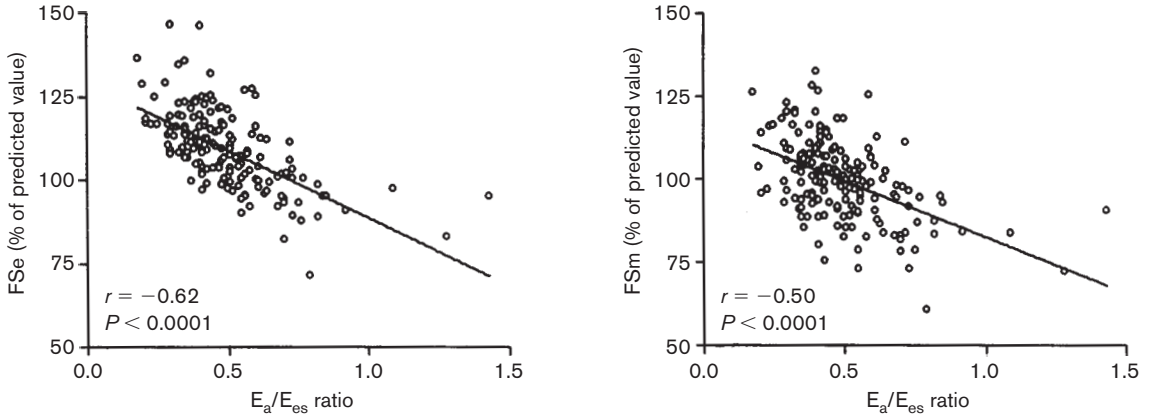
In comparison to hypertensives with normal E_aI, patients with elevated E_aI had similar left ventricular posterior wall thickness, greater septal thickness, smaller diastolic dimension and, as a consequence, higher relative wall thickness (Table 5). Both absolute and indexed left ventricular mass were significantly lower in the elevated E_aI group. Accordingly, left ventricular concentric remodelling was approximately fivefold more frequent in hypertensives with high E_aI than in those with normal E_aI (29 versus 6%, $P < 0.01$; Fig. 3).

Table 3 Relations of effective arterial elastance with left ventricular structure and function in normotensive and hypertensive individuals

	Posterior wall thickness	Relative wall thickness	Left ventricular mass	Endocardial FS	Midwall FS
Normotensive individuals					
E_a index	0.27*	0.62**	−0.17	−0.25*	−0.60**
Brachial systolic blood pressure	0.46**	0.43**	0.29**	0.20	−0.15
Brachial diastolic blood pressure	0.45**	0.31**	0.39**	−0.04	−0.27*
Carotid end-systolic pressure	0.49**	0.46**	0.31**	0.10	−0.26*
Hypertensive patients					
E_a index	0.19*	0.51**	−0.16*	−0.32**	−0.64**
Brachial systolic blood pressure	0.17*	0.03	0.19**	−0.02	−0.03
Brachial diastolic blood pressure	0.23**	−0.005	0.39**	−0.23**	−0.21**
Carotid end-systolic pressure	0.20**	0.002	0.30**	−0.10	−0.09

Data are means ± SD. FS, Fractional shortening; E_a, effective arterial elastance. * $P < 0.05$; ** $P < 0.01$.

Fig. 2



Univariate relation of endocardial (upper panel) and midwall (lower panel) fractional shortening expressed as percentage of the predicted value, and E_a/E_{es} ratio in hypertensive patients. Increasing E_a/E_{es} ratio, indicating that ventricular–vascular coupling is worse, is associated with lower fractional shortening. When E_a/E_{es} ratio approximates 0.5, midwall fractional shortening approximates 100% of the expected afterload-corrected value. Fse, Endocardial fractional shortening; FSm, mid-wall fractional shortening.

Table 4 Demographic and hemodynamic characteristics of hypertensive individuals with normal and high effective arterial elastance

	Normal E_aI ($\leqslant$ 3.43)	Elevated E_aI ($>$ 3.43)
Number	136	38
E_a (mmHg/ml)	1.5 ± 0.28	2.0 ± 0.5§
E_a index (mmHg/ml/m^2)	2.8 ± 0.4	3.9 ± 0.4§
Age (years)	56 ± 12†	55 ± 13
Sex (M/F)	80/56	28/10
Body mass index (kg/m^2)	26.4 ± 3.7	27.5 ± 4.8‡
Body surface area (m^2)	1.87 ± 0.23	1.95 ± 0.23†*
Brachial systolic blood pressure (mmHg)	158 ± 19‡	164 ± 22‡
Brachial diastolic blood pressure (mmHg)	93 ± 10‡	100 ± 11‡**
Brachial pulse pressure (mmHg)	65 ± 18‡	64 ± 19‡
Carotid peak systolic pressure (mmHg)	147 ± 17‡	156 ± 18‡**
Carotid end-diastolic pressure (mmHg)	92 ± 13‡	98 ± 15‡**
Carotid end-systolic pressure (mmHg)	125 ± 13‡	134 ± 15‡**
Carotid pulse pressure (mmHg)	55 ± 18†	58 ± 17‡
Heart rate (beats/min)	68 ± 11	68 ± 11
Augmentation index (%)	18 ± 11‡	19 ± 9‡

Data are means ± SD. E_a, effective arterial elastance. * $P < 0.05$, ** $P < 0.01$ versus hypertensives with normal E_aI. † $P < 0.05$, ‡ $P < 0.01$ versus normotensives (ANOVA, Dunnett's post-hoc test). § $P < 0.01$, by design.

While prevalence of concentric hypertrophy was similar between groups, the frequency of eccentric hypertrophy was twice as high in hypertensives with normal arterial elastance. Hypertensive individuals with high E_aI showed lower stroke index and cardiac index, markedly higher total peripheral resistance and lower endocardial as well as midwall fractional shortening, in spite of similar meridional and circumferential end-systolic stresses. When both indexes were expressed as percentages of predicted values, endocardial fractional shortening was normal while midwall fractional shortening was significantly depressed in hypertensives with elevated effective arterial elastance (Table 5). In this group, the ratio of arterial to ventricular elastance was significantly higher and the ratio of stroke volume to carotid pulse pressure was substantially lower than in hypertensives with normal E_aI (Table 5).

When compared to normotensive individuals, hypertensives with elevated effective arterial elastance showed smaller increases in left ventricular mass (LVM) (LVM/body surface area greater by 15 versus 27%; LVM/height$^{2.7}$ by 18 versus 31%; both $P < 0.001$) and more marked elevation of relative wall thickness (25 versus 12%; $P < 0.001$) than the group with normal E_aI (Table 5, Fig. 4). While left ventricular meridional end-systolic stress was normal in the group with normal E_aI and slightly elevated in hypertensive individuals with high E_aI, circumferential end-systolic stress was slightly and similarly elevated in both hypertensive groups (Table 5, Fig. 5). The stroke volume to pulse pressure ratio was significantly reduced only in hypertensive individuals with high E_aI. E_a/E_{es} ratio was normal in hypertensive individuals with normal E_aI and significantly increased in those with high E_aI.

Since age is a major determinant of E_aI in normal individuals [31], alternative analyses were performed using age-related upper normal limits to identify hypertensive patients with normal and high E_aI. These yelded similar results to these obtained using a single cutpoint.

Discussion

Effective arterial elastance and left ventricular afterload in hypertension

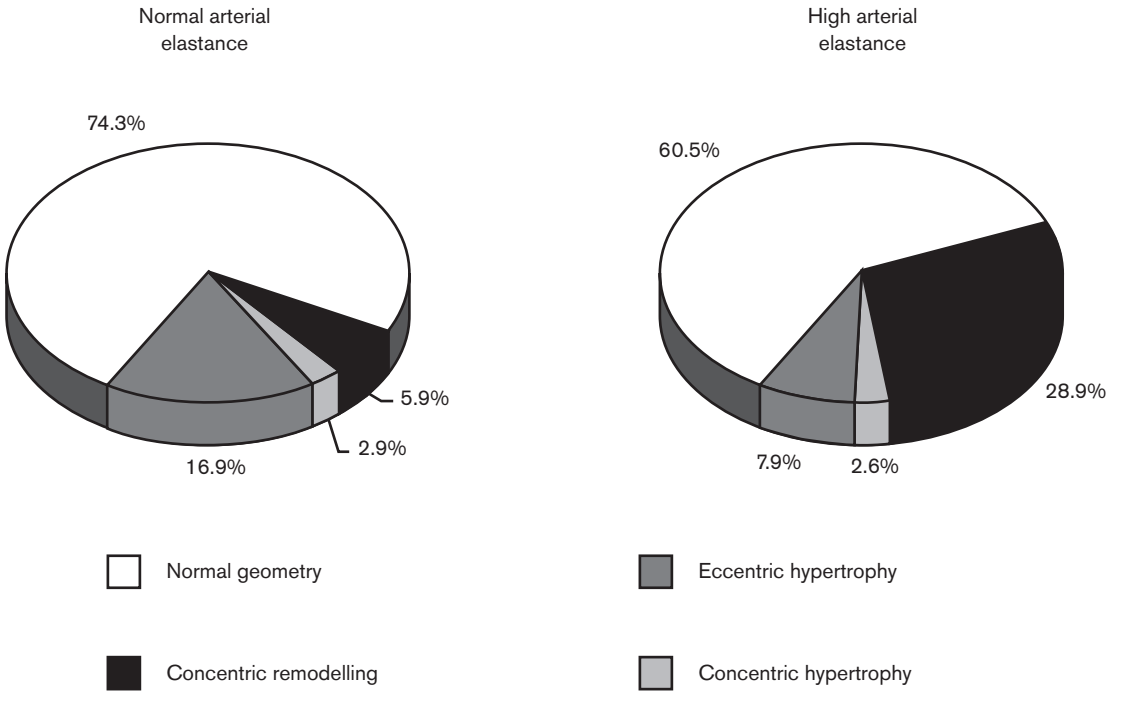
Aortic impedance, i.e. the relationship between pulsatile pressure and flow in the aorta analysed in the

Table 5 Left ventricular anatomy and function in hypertensive patients with normal and high effective arterial elastance

	Normal E_aI ($\leq$ 3.43)	Elevated E_aI ($>$ 3.43)
Left ventricular posterior wall thickness (cm)	0.94 ± 0.12‡	0.97 ± 0.12‡
Inter-ventricular diastolic septal thickness (cm)	0.99 ± 0.13‡	1.05 ± 0.14‡**
Left ventricular diastolic diameter (cm)	5.11 ± 0.50	4.74 ± 0.46**
Left ventricular mass/BSA (g/m^2)	96.8 ± 19.3‡	87.5 ± 18.5‡**
Left ventricular mass/height$^{2.7}$ ($g/m^{2.7}$)	43.9 ± 9.0‡	39.5 ± 9.2‡**
Left ventricular relative wall thickness	0.37 ± 0.05‡	0.41 ± 0.06‡**
Stroke index (M-mode) (ml/m^2)	46.0 ± 7.6‡	34.2 ± 5.4‡**
Stroke index (Doppler) (ml/m^2) $n = 42$	43.9 ± 8.2	37.7 ± 7.7*
Cardiac index ($l/min/m^2$)	3.1 ± 0.7‡	2.3 ± 0.5‡**
Total peripheral resistance (dynes/cm sec^{-5})	1658 ± 371	2247 ± 408‡**
Stroke volume/carotid pulse pressure (ml/mmHg)	1.74 ± 0.72	1.25 ± 0.43‡**
Meridional end-systolic stress ($kdynes/cm^2$)	72.2 ± 20.8	76.7 ± 24.7‡
Circumferential end-systolic stress ($kdynes/cm^2$)	199 ± 49‡	210 ± 59‡
Endocardial fractional shortening (%)	38.9 ± 5.0	35.1 ± 5.1†**
Stress-corrected endocardial shortening (%)	110.8 ± 11.0‡	102.3 ± 11.1**
Midwall fractional shortening (%)	18.4 ± 2.0	15.8 ± 2.0‡**
Stress-corrected midwall shortening (%)	102.5 ± 10.6	89.2 ± 11.5‡**
E_{es} (mmHg/ml)	3.5 ± 1.5‡	3.8 ± 1.3‡
E_a/E_{es}	0.47 ± 0.16	0.58 ± 0.20†**

Data are means ± SD. E_{es}, Left ventricular end-systolic elastance (single-point estimate); E_a, effective arterial elastance. * $P < 0.05$, ** $P < 0.01$ versus hypertensives with normal E_aI. † $P < 0.05$, ‡ $P < 0.01$ versus normotensives (ANOVA, Dunnett's post-hoc test).

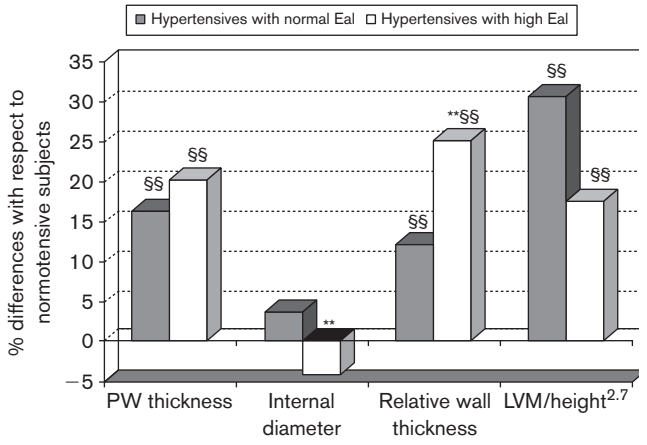
Fig. 3



Patterns of left ventricular geometry in hypertensives with normal and high effective arterial elastance. Prevalence of concentric remodelling was significantly greater in hypertensive patients with high arterial elastance. Pearson's chi-squared = 16.9; $P < 0.0008$.

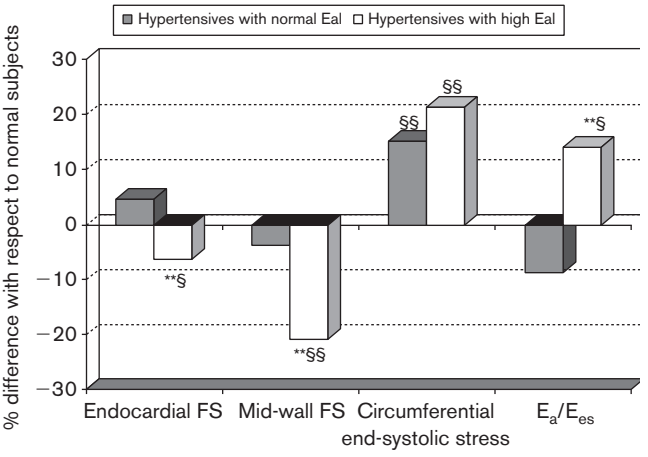
frequency domain [38], is considered the most accurate index of left ventricular afterload, since it comprises the steady as well as pulsatile component of vascular load [5,6,38]. However, its use in the clinical setting is made difficult by the need of invasive measurements of pressure and flow. Effective arterial elastance is a simpler parameter that also incorporates both steady and pulsatile components of arterial load [8,9]. A previous study has shown its reliability in estimating arterial load also when steady-state parameters (stroke volume and end-systolic pressure) are used in its calculation instead of simultaneous pressure/volume

Fig. 4



Left ventricular anatomy in hypertensive individuals with normal and high effective arterial elastance. Data are expressed as percentage differences with respect to normotensive controls (ANOVA). * $P < 0.05$ and ** $P < 0.01$ versus hypertensive individuals with normal effective arterial elastance (Sheffé's post-hoc test). § $P < 0.05$ and §§ $P < 0.01$ versus normotensive controls (Dunnett's post-hoc test). PW, Posterior wall; LVM, left ventricular mass.

Fig. 5



Left ventricular function and ventricular–vascular coupling in hypertensive individuals with normal and high effective arterial elastance. Data are expressed as percentage differences with respect to normotensive controls (ANOVA). * $P < 0.05$ and ** $P < 0.01$ versus hypertensive individuals with normal effective arterial elastance (Sheffé's post-hoc test). § $P < 0.05$ and §§ $P < 0.01$ versus normotensive controls (Dunnett's post-hoc test). FS, Fractional shortening; E_{es}, left ventricular end-systolic elastance (single-point estimate); E_a, effective arterial elastance.

loops and vascular impedance parameters [7]. In the present investigation, we used fully non-invasive techniques to assess effective arterial elastance and its impact on left ventricular geometry and systolic function in uncomplicated essential hypertension.

In agreement with a recent report [34], our data show that effective arterial elastance is, on average, increased in hypertension. However, the present study also demonstrates that E_a falls within the normal range in most hypertensive individuals. Only a minority of patients (22%) have abnormally elevated effective arterial elastance, a finding which is associated with higher diastolic blood pressure and total peripheral resistance. Although no age difference was present between hypertensive patients with normal and high E_aI, based on a previous observation that age is a major determinant of E_aI [31], alternative analyses were performed using age-dependent cutpoints for identifying patient subgroups that yielded similar patient distribution and characteristics. The presence of different hemodynamic features in these two groups of hypertensive patients suggests that different mechanisms participate in the genesis of hypertension in them. In fact, while patients with normal effective arterial elastance had only 7% higher total peripheral resistance and 19% higher cardiac index than the normotensive individuals, the group with elevated effective arterial elastance had markedly increased peripheral resistance, reduced cardiac index and stiffer arterial tree, as revealed by lower stroke volume/pulse pressure ratio.

The potential effect of pressure wave reflection on effective arterial elastance should be considered. It is known that stiffening of the arterial system generates earlier reflected pressure waves that reach the heart during ejection and boost systolic pressure [30]. In the setting of early wave reflection due to hypertension, end-systolic pressure might be less affected than peak systolic pressure, resulting in lower values of effective arterial elastance and underestimation of the actual arterial load. To explore this potentially confounding factor, we measured the augmentation index, which is known to reflect both intensity and timing of the reflected pressure wave [29,30]. Augmentation index was significantly ($P < 0.001$) and positively related to both end-systolic pressure and arterial elastance in the whole hypertensive population, and similarly increased in the two hypertensive groups compared to normotensive individuals (Table 4). This suggests that the contribution of enhanced wave reflection to arterial load is of the same extent in the two hypertensive groups, and it is not likely to be responsible for the observed differences in E_aI. It is somewhat surprising that the group with a stiffer arterial tree, as revealed by increased E_aI and reduced stroke volume/pulse pressure ratio, does not exhibit higher levels of augmentation index than hypertensives with normal E_aI and presumably more compliant arteries. This may reflect the compensatory effect of a slightly higher prevalence of women in the latter group (41 versus 26%), since female sex has been associated with earlier pressure wave reflection [39].

Effective arterial elastance and left ventricular geometry

As previously reported [34], increased effective arterial elastance was associated with higher left ventricular relative wall thickness. In contrast, left ventricular mass increased less in hypertensives with elevated than in those with normal effective arterial elastance, in the setting of similar brachial systolic but higher diastolic pressure. The direct relation of E_aI with relative wall thickness (Table 3) provides evidence that an elevated arterial load is a major stimulus to the development of left ventricular concentric remodelling. In fact, left ventricular concentric remodelling was fivefold more frequent in hypertensives with high than in those with normal arterial elastance. Although an autocorrelation phenomenon between M-mode-derived stroke volume and left ventricular dimension is expected and might potentially account for the positive relations of left ventricular geometry with E_aI, a significant relation of E_aI with relative wall thickness ($r = 0.36$) persisted in the subset of individuals in whom Doppler-derived stroke volume was used to assess E_aI. Since left ventricular wall stress did not differ between the two groups, left ventricular geometric adaptation was similarly compensatory for the higher vascular load in hypertensives with high arterial elastance as in those with normal arterial elastance.

Ventricular–vascular coupling and left ventricular function in hypertension

In this study we used an estimation of left ventricular maximal elastance based on a single-point determination of end-systolic pressure to volume ratio. It is known that both time-varying and single beat-determined left ventricular maximal elastance are load dependent [40–42]. We do not have information about either ventricular preload or the response of ventricular elastance to manipulation of loading conditions in our individuals and thus we can not make precise inferences about left ventricular contractility on the basis of this estimate of E_{es}. However, considering the single point-determined E_{es} as an index of the ability of the left ventricle to empty opposed to a given pressure [42] instead of an intrinsic property of the cardiac muscle, we used this index in the evaluation of ventricular-vascular coupling, as suggested in a previous study [34]. Both in normotensive and hypertensive individuals the E_a/E_{es} ratio was on average close to 0.50, similar to previously reported normal values [10,11] which indicate optimal ventricular–vascular coupling in the whole hypertensive group. However, patients with elevated E_aI had a significantly increased E_a/E_{es} ratio, consistent with sub-optimal ventricular–vascular coupling and mechanical efficiency. The altered ventricular–vascular coupling could be responsible for the lower left ventricular myocardial function in hypertensives with high effective arterial elastance. In fact, significant inverse relationships were present between the E_a/E_{es} ratio and both endocardial and midwall fractional shortening, expressed as percentages of the predicted values for the observed level of end-systolic stress. Moreover, while the hypertensive group with normal E_aI and optimal ventricular–vascular coupling had supra-normal endocardial fractional shortening and normal midwall fractional shortening, the group of patients with elevated E_aI and sub-optimal ventricular–vascular coupling showed a lower level of midwall fractional shortening, while endocardial fractional shortening was normal. These data are consistent with previous observations that hypertensive individuals with depressed left ventricular midwall shortening have a stiffer arterial tree, concentric left ventricular geometry and increased total peripheral resistance [22] and that shortening at the endocardial level is preserved by the concentric ventricular geometry [43]. The association between elevated effective arterial elastance, an indicator of structural and/or functional arterial alterations [31], and concentric left ventricular geometry could explain the greater incidence of vascular disease [44] and vascular events [45,46] in hypertensives with this geometric pattern compared to those with similar levels of left ventricular mass but normal relative wall thickness.

In conclusion, these data, as well as previous reports [26,44,47], provide evidence of a close interaction between the left ventricle and arterial tree. Structural and functional arterial modifications increase the vascular load on the left ventricle and play a role in inducing concentric left ventricular remodelling or hypertrophy that is initially adaptive but ultimately predisposes to systolic dysfunction [22] and clinical cardiovascular disease [45,46].

References

1 Ganau A, Devereux RB, Roman MJ, de Simone G, Pickering TG, Saba PS, *et al*. Patterns of left ventricular hypertrophy and geometric remodeling in essential hypertension. *J Am Coll Cardiol* 1992; **19**:1550–1558.

2 Ganau A, Devereux RB, Pickering TG, Roman MJ, Schnall PL, Santucci S, *et al*. Relation of left ventricular hemodynamic load and contractile performance to left ventricular mass in hypertension. *Circulation* 1990; **81**:25–36.

3 Ganau A, Arru A, Saba PS, Piga G, Glorioso N, Tonolo G, *et al*. Stroke volume and left heart anatomy in relation to plasma volume in essential hypertension. *J Hypertens* 1991; **9 (suppl 6)**:S150–S151.

4 Bouthier JD, De Luca N, Safar ME, Simon A. Cardiac hypertrophy and arterial distensibility in essential hypertension. *Am Heart J* 1985; **109**:1345–1352.

5 Ting CT, Brin KP, Lin SJ, Wang SP, Chang MS, Chiang MN, *et al*. Arterial hemodynamics in human hypertension. *J Clin Invest* 1986; **78**:1462–1471.

6 O'Rourke MF. Arterial hemodynamics in hypertension. *Circ Res*, 1970; **26/27 (suppl II)**:II123–II133.

7 Kelly RP, Ting CT, Yang TM, Liu CP, Maughan L, Chang MS, *et al*. Effective arterial elastance as an index of arterial vascular load in humans. *Circulation* 1992; **86**:513–521.

8 Sunagawa K, Maughan L, Burkoff D, Sagawa K. Left ventricular interaction with arterial load studied in isolated canine ventricle. *Am J Physiol* 1983; **245**:H773–H780.

9 Sunagawa K, Maughan WL, Sagawa K. Optimal arterial resistance for the maximal stroke work studied in isolated canine left ventricle. *Circ Res* 1985; **56**:586–595.

10 Sasayama S, Asanoi H. Coupling between the heart and arterial system in heart failure. *Am J Med*, 1991; **90 (suppl 5B)**:5B14S–5B18S.

11 Starling MR. Left ventricular-arterial coupling relations in the normal human heart. *Am Heart J* 1993; **125**:1659–1666.
12 Sahn DJ, De Maria A, Kisslo J, Weyman A. Recommendations regarding quantitation in M-mode echocardiography: results of a survey of echocardiographic measurements. *Circulation* 1978; **58**:1072–1083.
13 Schiller NB, Shah PM, Crawford M, De Maria A, Devereux RB, Feigenbaum H, *et al*. Recommendation for quantitation of the left ventricle by two-dimensional echocardiography. *J Am Soc Echo* 1989; **2**:358–367.
14 Devereux RB, Reichek N. Echocardiographic determination of left ventricular mass in man: anatomic validation of the method. *Circulation* 1977; **55**:613–618.
15 Devereux RB, Alonso DR, Lutas EM, Gottlieb GJ, Campo E, Sachs I, *et al*. Echocardiographic assessment of left ventricular hypertrophy: comparison to necropsy findings. *Am J Cardiol* 1986; **57**:450–458.
16 de Simone G, Daniels SR, Devereux RB, Meyer RA, Roman MJ, deDivitiis O, *et al*. Left ventricular mass and body size in normotensive children and adults: assessment of allometric relations and impact of overweight. *J Am Coll Cardiol* 1992; **20**:1251–1260.
17 Devereux RB, James GD, Pickering TG. What is normal blood pressure? Comparison of ambulatory pressure level and variability in patients with normal or abnormal left ventricular geometry. *Am J Hypertens* 1993; **6**:211S–215S.
18 Ganau A, Saba PS, Roman MJ, de Simone G, Realdi G, Devereux RB. Ageing induces left ventricular concentric remodelling in normotensive subjects. *J Hypertens* 1995; **13**:1818–1822.
19 Teichholz LE, Kreulen T, Herman MV, Gorlin R. Problems in echocardiographic volume determinations: echocardiographic-angiographic correlations in the presence or absence of asynergy. *Am J Cardiol* 1976; **37**:7–11.
20 Dubin J, Wallerson DC, Cody RJ, Devereux RB. Comparative accuracy of Doppler echocardiographic methods for clinical stroke volume determination. *Am Heart J* 1990; **120**:116–123.
21 Gaasch WH, Zile MR, Hoshino PK, Apstein CS, Blaustein AS. Stress-shortening relations and myocardial blood flow in compensated and failing canine hearts with pressure-overload hypertrophy. *Circulation* 1989; **79**:872–883.
22 de Simone G, Devereux RB, Roman MJ, Ganau A, Saba PS, Alderman MH, *et al*. Assessment of left ventricular function by the midwall fractional shortening/end-systolic stress relation in human hypertension. *J Am Coll Cardiol* 1994; **23**:1444–1451.
23 Randall OS, Westerhof N, van den Bos GC, Alexander B. Reliability of stroke volume to pulse pressure ratio for estimating and detecting changes in arterial compliance. *J Hypertens* 1986; **4 (suppl 5)**:S293–S296.
24 Chemla D, Hebert J-L, Coirault C, Zamani K, Suard I, Colin P, *et al*. Total arterial compliance estimated by stroke volume-to-aortic pulse pressure ratio in humans. *Am J Physiol* 1998; **274**:H500–H505.
25 Roman MJ, Pini R, Pickering TG, Devereux RB. Noninvasive measurements of arterial compliance in hypertensive compared with normotensive adults. *J Hypertens*, 1992; **10 (suppl 6)**:S115–S118.
26 Roman MJ, Saba PS, Pini R, Spitzer M, Pickering TG, Rosen S, *et al*. Parallel cardiac and vascular adaptation in hypertension. *Circulation* 1992; **86**:1909–1918.
27 Saba PS, Roman MJ, Pini R, Spitzer M, Ganau A, Devereux RB. Relation of pressure waveform to left ventricular and carotid anatomy in normotensive subjects. *J Am Coll Cardiol* 1993; **22**:1873–1880.
28 Drzewiecki GM, Melbin J, Noordergraaf A. Arterial tonometry: review and analysis *J Biomech* 1983; **16**:141–152.
29 Kelly R, Hayward C, Ganis J, Daley J, Avolio A, O'Rourke M. Noninvasive registration of the arterial pressure pulse waveform using high-fidelity applanation tonometry. *J Vasc Med Biol* 1989; **1**:142–149.
30 Murgo JP, Westerhof N, Giolma JP, Altobelli SA. Aortic input impedance in normal man: relationship to pressure wave forms. *Circulation* 1981; **62**:105–116.
31 Saba PS, Roman MJ, Ganau A, Pini R, Jones EC, Pickering TG, *et al*. Relations of effective arterial elastance to demographic and arterial characteristics in normotensive and hypertensive adults. *J Hypertens* 1995; **13**:971–977.
32 McKay RG, Aroesty JM, Heller GV, Royal HD, Warren SE, Grossman W. Assessment of the end-systolic pressure-volume relationship in human beings with the use of a time-varying elastance model. *Circulation* 1986; **74**:97–104.
33 Asanoi H, Sasayama S, Kameyama T. Ventriculo-arterial coupling in normal and failing heart in humans. *Circ Res* 1989; **65**:483–493.
34 Cohen-Solal A, Caviezel B, Himbert D, Gourgon R. Left ventricular-arterial coupling in systemic hypertension: analysis by means of arterial effective and left ventricular elastances *J Hypertens* 1994; **12**:591–600.
35 Wallerson DC, Ganau A, Roman MJ, Devereux RB. Measurement of cardiac output by M-mode and two-dimensional echocardiography: application to patients with hypertension. *Eur Heart J* 1990; **11 (suppl I)**:67–78.
36 Devereux RB, Roman MJ, Paranicas M, O'Grady MJ, Wood EA, Howard BV, *et al*. Relations of Doppler stroke volume and its components to left ventricular stroke volume in normotensive and hypertensive American Indians: The Strong Heart Study. *Am J Hypertens* 1997; **10**:619–628.
37 Bland JM, Altman DG. Comparing methods of measurement: why plotting difference against standard method is misleading. *Lancet* 1995; **346**:1085–1087.
38 O'Rourke MF. Vascular impedance in studies of arterial and cardiac function. *Physiol Rev* 1982; **62**:570–623.
39 Hayward CS, Kelly RP. Gender-related differences in the central arterial pressure waveform. *J Am Coll Cardiol* 1997; **30**:1863–1871.
40 van der Linden LP, van der Velde ET, van Houwelingen HC, Bruschke AV, Baan J. Determinants of end-systolic pressure during different load conditions in the in situ left ventricle. *Am J Physiol*, 1994; **267**:H1895–H1906.
41 Starling MR, Montgomery DG, Walsh RA. Load dependence of the single beat maximal pressure (stress)/volume ratios in humans. *J Am Coll Cardiol* 1989; **14**:345–353.
42 Carabello BA. Ratio of end-systolic stress to end-systolic volume: it is a useful clinical tool? *J Am Coll Cardiol* 1989; **14**:496–498.
43 Aurigemma GP, Silver KH, Priest MA, Gaasch WH. Geometric changes allow normal ejection fraction despite depressed myocardial shortening in hypertensive left ventricular hypertrophy. *J Am Coll Cardiol* 1995; **26**:195–202.
44 Roman MJ, Pickering TG Schwartz JE, Pini R, Devereux RB. Relation of arterial structure and function to left ventricular geometric patterns in hypertensive adults. *J Am Coll Cardiol* 1996; **28**:751–756.
45 Koren MJ, Devereux RB, Casale PN, Savage DD, Laragh JH. Relation of left ventricular mass and geometry to morbidity and mortality in men and women with essential hypertension *Ann Intern Med* 1991; **114**:345–352.
46 Verdecchia P, Schillaci G, Borgioni C, Ciucci A, Battistelli M, Bartoccini C, *et al*. Adverse prognostic significance of concentric remodeling of left ventricle in hypertensive patients with normal left ventricular mass. *J Am Coll Cardiol* 1995; **25**:871–878.
47 Roman MJ, Pickering TG, Schwartz JE, Pini R, Devereux RB. Association of carotid atherosclerosis and left ventricular hypertrophy. *J Am Coll Cardiol* 1995; **25**:83–90.