JACC Vol. 28, No. 3
September 1996:751–6

Relation of Arterial Structure and Function to Left Ventricular Geometric Patterns in Hypertensive Adults

MARY J. ROMAN, MD, FACC, THOMAS G. PICKERING, MD, PHD, JOSEPH E. SCHWARTZ, PHD, RICCARDO PINI, MD, RICHARD B. DEVEREUX, MD, FACC

New York, New York

Objectives. **The present study sought to determine whether conduit artery structure and function vary according to the pattern of left ventricular adaptation to hypertension.**

Background. **Although left ventricular geometric pattern has been shown to predict cardiovascular events in hypertension, the arterial status in patients with the different patterns is unknown.**

Methods. **We evaluated arterial structure and function by carotid ultrasound and applanation tonometry in 271 unmedicated hypertensive patients classified by echocardiography as having normal ventricular geometry (n = 176), concentric remodeling (n = 54), concentric hypertrophy (n = 16) or eccentric hypertrophy (n = 25).**

Results. **All groups were similar in age, gender distribution and body size. Patients with concentric and eccentric hypertrophy had similar blood pressures (mean 173/100 and 171/99 mm Hg, respectively) and left ventricular mass, but compared with patients with normal left ventricular geometry and concentric remodeling, only those with concentric hypertrophy had increased arterial wall thickness (0.96 ± 0.20 vs. 0.80 ± 0.18 mm, $p < 0.05$), end-diastolic diameter (6.38 ± 0.97 vs. 5.76 ± 0.87 mm, $p < 0.05$), cross-sectional area (22.1 ± 5.71 vs. 16.6 ± 5.4 mm^2, $p < 0.05$) and elastic modulus (713 ± 265 vs. 471 ± 241 dynes/$cm^2 \times 10^{-6}$, $p < 0.05$). Patients with concentric remodeling and eccentric hypertrophy had similar values for these measures (0.85 ± 0.22 and 0.89 ± 0.21 mm, 5.67 ± 0.77 and 6.04 ± 0.44 mm, 17.2 ± 5.4 and 19.7 ± 5.9 mm^2, 558 ± 263 and 614 ± 257 dynes/$cm^2 \times 10^{-6}$, respectively), despite lower systolic blood pressures in the former group (156/94 mm Hg, $p < 0.001$). The prevalence of plaque was comparable in patients with concentric (56%) and eccentric (42%) hypertrophy and significantly greater in those with normal geometry (21%).**

Conclusions. **Among patients with generally mild, uncomplicated systemic hypertension, arterial structure and function are most abnormal when concentric left ventricular hypertrophy is present and may contribute to the more adverse outcome associated with this geometric pattern.**

(J Am Coll Cardiol 1996;28:751–6)

Recent studies have challenged the traditional concept that the heart consistently responds to systemic hypertension by developing concentric left ventricular hypertrophy and have demonstrated a wider spectrum of left ventricular geometric patterns in hypertensive patients (1–7). Classification of patients based on whether left ventricular muscle mass and the left ventricular wall thickness/chamber radius ratio ("relative wall thickness" [8]) are normal or abnormal yields four groups with different left ventricular geometric patterns: normal geometry (normal mass and relative wall thickness), concentric hypertrophy (an increase in both left ventricular mass with normal relative wall thickness), eccentric hypertrophy (increased left ventricular mass with normal wall thickness) and the recently identified pattern of concentric left ventricular remodeling (increased relative wall thickness with normal mass [1]). Studies that have grouped hypertensive patients by these geometric patterns have revealed distinctive profiles of systemic hemodynamics (1,5), ambulatory blood pressure (3), plasma volume (9), myocardial performance (5) and prognosis (2,7).

However, no information is currently available on whether hypertensive patients with different left ventricular geometric patterns also differ with regard to the structure and function of their systemic arterial tree. Indirect support for this possibility is provided by evidence from several laboratories of relations between arterial geometry and function and left ventricular structure, which remain significant after adjustment for the effects of age, gender and arterial pressure (10–14). Accordingly, the present study was undertaken to examine arterial structure and function by ultrasound and applanation tonometry of the extracranial carotid arteries in unmedicated hypertensive adults with echocardiographically classified left ventricular geometric patterns. In addition, the relation of left ventricular geometric pattern to carotid atherosclerosis was determined in view of the recent observations of increasing risk of stroke with increasing quartile of left ventricular mass (15)

From the Department of Medicine and the Cardiovascular Center, The New York Hospital–Cornell Medical Center, New York, New York. This study was supported in part by Grants HL 18323, 30605 and 47540 from the National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, Maryland.

Manuscript received December 27, 1995; revised manuscript received April 8, 1996, accepted April 16, 1996.

Address for correspondence: Dr. Mary J. Roman, Division of Cardiology, Box 222, The New York Hospital–Cornell Medical Center, 525 East 68th Street, New York, New York 10021.

0735-1097/96/$15.00
PII S0735-1097(96)00225-2

and the independent association of increased left ventricular mass with the presence of carotid atherosclerosis (14,16).

Methods

Patients. Hypertensive patients were eligible for the study if they 1) had no clinical evidence of cardiac or cerebrovascular disease; 2) had no evidence of valvular heart disease on imaging and Doppler echocardiography; 3) were either previously unmedicated or had been free of antihypertensive medications for at least 3 weeks (with periods ranging up to 6 years); and 4) had technically satisfactory echocardiograms and carotid ultrasound studies. Hypertension was documented by systolic arterial blood pressure >140 mm Hg (>160 mm Hg in subjects ≥65 years old) or diastolic arterial blood pressure 90 mm Hg, or both, on the average of multiple determinations by arm-cuff and mercury manometry. Subjects consisted of hypertensive members of a work site–based sample of employed adults or patients undergoing diagnostic evaluation of their hypertension at The New York Hospital–Cornell Medical Center, as previously described in part (14,17).

Echocardiographic methods. M-mode and two-dimensional echocardiograms were performed by a skilled research technician using previously described methods (18). M-mode stripchart recordings of the left ventricle on up to six high quality cycles were coded and read blindly by a single investigator (M.J.R.) using a digitizing tablet. Penn convention measurements were used to calculate left ventricular mass (19,20), which was indexed for body surface area. American Society of Echocardiography measurements (21) were used for left ventricular chamber diameter, wall thickness and relative wall thickness. When the M-mode beam could not be oriented along the left ventricular minor axis from available chest wall acoustic windows, measurements made by the American Society of Echocardiography recommendations for two-dimensional echocardiography (22) were substituted. Brachial blood pressure was taken at the end of the echocardiographic examination.

Partition values used to classify left ventricular geometric patterns were the same as those previously used for comparison with ambulatory blood pressures (3). Patients were classified as abnormal if the left ventricular relative wall thickness exceeded 0.41 (1) or if the left ventricular mass index exceeded 108 g/m^2 in women or 118 g/m^2 in men (23).

Carotid ultrasound. As previously described (10,14), a 7.5-MHz duplex transducer was used to scan the common, internal and external carotid arteries for discrete atherosclerotic plaques (24). Two-dimensionally guided M-mode recordings of the distal common carotid artery were recorded on videotape and subsequently digitized using a frame grabber and customized software (ARTSS Cornell Research Foundation). Electronic calipers were used to measure the internal diameter (D_d) and far wall intimal-medial thickness (IMT_d) (25) at end-diastole, recognized from the nadir of the simultaneous arterial pressure waveform or the minimal arterial diameter, as well as the diameter at peak systole (D_s). Arterial geometry was further characterized by calculation of the arterial relative wall thickness (RWT_{art}) as

$$RWT_{art} = 2 * IMT_d/D_d$$

and of the arterial cross-sectional area (CSA) as

$$CSA = \pi * (IMT_d + [D_d/2])^2 - \pi * (D_d/2)^2.$$

Arterial function assessment. A high fidelity arterial pressure waveform was recorded noninvasively by placing a solid-state Millar transducer over the right common carotid artery while recording M-mode images of the left common carotid artery, as previously described (26). Orientation and pressure applied to the transducer were adjusted to achieve applanation of the artery between the transducer and the underlying tissue, as has been validated to yield accurate estimates of intraarterial pulse pressure by comparison with simultaneous invasive pressure recordings (27,28). Systolic and diastolic carotid artery pressures were derived by calibrating the electronic mean of the carotid artery pressure waveform using the mean brachial artery pressure derived from the arm-cuff and mercury manometer measurements (26).

Arterial strain, the percent systolic expansion of the arterial lumen, was calculated as

$$Strain = ([D_s - D_d]/D_d) * 100.$$

Carotid pressures, D_d, D_s and IMT_d were used to calculate several measures of arterial stiffness. Peterson's elastic modulus (E_p) (29) was calculated as

$$E_p = ([P_s - P_d]/[D_s - D_d]) * D_d,$$

where P_s and P_d are the carotid systolic and diastolic pressures, respectively. Young's modulus (E) (30) was calculated as

$$E = ([P_s - P_d]/[D_s - D_d]) * ([D_d + D_s]/[IMT_d]).$$

Carotid artery stiffness was also calculated using a pressure-independent measure (β) (31,32):

$$\beta = (\ln[P_s - P_d]) * ([D_s - D_d]/D_d).$$

These measures provide indexes of regional arterial stiffness under the vessel's usual loading conditions (E_p) or which adjust for the effects of arterial wall thickening (E) and distending pressure (β).

Statistical methods. Statistical analyses were performed using SPSS, Release 6.1. Data are presented as the mean value ± SD. Continuous variables were compared by one-way analysis of variance followed by the Scheffé post hoc test for multiple comparisons. The normality of distribution of variables was assessed by the Kolmogorov-Smirnov or Shapiro-Wilks test; variables found to deviate from normality were log-transformed before application of statistical tests. Proportions were compared among groups by the chi-square statistic. The null hypothesis was rejected at $p < 0.05$.

Results

Patient characteristics (Table 1). The 271 subjects had a mean age of 55 ± 12 years (range 25 to 88). Patients in the four

Table 1. Demographic and Clinical Variables

Variable	Normal Geometry (n = 176)	Concentric Remodeling (n = 54)	Eccentric Hypertrophy (n = 25)	Concentric Hypertrophy (n = 16)	Overall p Value
Age (yr)	53.5 ± 11.3	57.3 ± 12.7	57.5 ± 10.6	58.2 ± 12.7	0.07
Gender (% male)	61	65	64	69	0.91
Race (% white)	71	57	64	38	0.18
BSA (m^2)	1.89 ± 0.22	1.88 ± 0.23	1.90 ± 0.25	1.89 ± 0.27	0.99
BMI (kg/m^2)	26.5 ± 3.8	27.1 ± 4.9	27.6 ± 4.1	27.4 ± 4.9	0.47
Blood pressure (mm Hg)					
Systolic	151 ± 18	156 ± 20	171 ± 30*†	173 ± 21*†	< 0.0001
Diastolic	91 ± 9	94 ± 12	99 ± 13‡	100 ± 16‡	< 0.0001
Total cholesterol (mg/dl)	222 ± 42	223 ± 42	237 ± 53	224 ± 51	0.55
HDL cholesterol (mg/dl)	55 ± 16	55 ± 16	54 ± 17	50 ± 18	0.75
Serum creatinine (mg/dl)	1.0 ± 0.2	1.1 ± 0.2	1.0 ± 0.2	1.0 ± 0.2	0.17
Smoking (% former or current)	44	47	48	25	0.44

*$p < 0.001$ versus normal geometry. †$p < 0.001$ versus concentric remodeling. ‡$p < 0.05$ versus normal geometry. Data are presented as mean value ± SD or percent of patients. BSA = body surface area; BMI = body mass index; HDL = high density lipoprotein.

groups characterized by different left ventricular geometric patterns were similar regarding gender distribution, body size, serum lipids and smoking history. Although race did not significantly differ among the groups, patients with concentric hypertrophy were predominantly African-American or African-Caribbean. Likewise, there were no differences in serum creatinine in this healthy group. Patients with either pattern of left ventricular hypertrophy had substantially elevated brachial systolic and diastolic pressures.

Left ventricular structure (Table 2). By definition, left ventricular mass was increased in the groups with concentric and eccentric hypertrophy, whereas relative wall thickness was increased in the groups with the two concentric patterns. Left ventricular end-diastolic diameter was significantly reduced in the concentric remodeling group in comparison with the three other groups, whereas left ventricular end-diastolic diameter was significantly increased in the eccentric hypertrophy group in comparison with all the other groups.

Carotid artery structure (Table 3, Fig. 1). Compared with patients with normal left ventricular geometry, only patients with concentric hypertrophy demonstrated significant increases in carotid artery size, as evidenced by end-diastolic diameter, cross-sectional area and intimal-medial thickness. Patients with concentric hypertrophy, likewise, had significant increases in arterial diameter and cross-sectional area compared with those with concentric remodeling. Despite substantially higher systolic and diastolic pressures, arterial structure in patients with eccentric hypertrophy was similar to that in patients with normal geometry and concentric remodeling. The prevalence of plaque was significantly increased in the two hypertrophy groups.

Arterial function (Table 4). Vascular strain was lowest and elastic modulus highest in patients with concentric hypertrophy. However, when structural adaptation (wall thickening) and distending pressure were considered by Young's modulus and β, respectively, differences between the four groups were no longer statistically significant.

Discussion

Left ventricular geometry and carotid hypertrophy. Although classification of left ventricular geometric patterns in patients with hypertension strongly predicts the incidence of subsequent vascular events (2,7,33,34), little is known about arterial structure and function in patients with different left ventricular geometric adaptations. The principal new findings

Table 2. Left Ventricular Structure and Function

Variable	Normal Geometry (n = 176)	Concentric Remodeling (n = 54)	Eccentric Hypertrophy (n = 25)	Concentric Hypertrophy (n = 16)	Overall p Value
End-diastolic diameter (cm)	5.03 ± 0.43*	4.54 ± 0.33	5.63 ± 0.45*†‡	5.21 ± 0.37*	< 0.0001
Fractional shortening (%)	38 ± 5	39 ± 6	34 ± 7§‖	38 ± 5	< 0.005
Septal thickness (cm)	0.93 ± 0.11	1.06 ± 0.10†	1.08 ± 0.13†	1.21 ± 0.14†*¶	< 0.0001
Posterior wall thickness (cm)	0.87 ± 0.09	1.02 ± 0.07†	1.01 ± 0.10†	1.15 ± 0.10†*¶	< 0.0001
Relative wall thickness	0.35 ± 0.03	0.45 ± 0.04†#	0.36 ± 0.04	0.44 ± 0.02†#	< 0.0001
Mass (g)	161.6 ± 38.3	164.8 ± 28.6	236.7 ± 47.5*†	246.8 ± 55.1*†	< 0.0001
Mass index (g/m^2)	85.1 ± 15.3	87.6 ± 11.2	123.6 ± 11.8*†	129.1 ± 13.2*†	< 0.0001

*$p < 0.001$ versus concentric remodeling. †$p < 0.001$ versus normal geometry. ‡$p < 0.05$ versus concentric hypertrophy. §$p < 0.01$ versus normal geometry. ‖$p < 0.005$ versus concentric remodeling. ¶$p < 0.01$ versus eccentric hypertrophy. #$p < 0.001$ versus eccentric hypertrophy. Data are presented as mean value ± SD.

Table 3. Carotid Artery Structure

Variable	Normal Geometry (n = 176)	Concentric Remodeling (n = 54)	Eccentric Hypertrophy (n = 25)	Concentric Hypertrophy (n = 16)	Overall p Value
End-diastolic diameter (mm)	5.76 ± 0.87	5.67 ± 0.77	6.04 ± 0.44	6.38 ± 0.97*†	< 0.01
Intimal-medial thickness (mm)	0.80 ± 0.18	0.85 ± 0.22	0.89 ± 0.21	0.96 ± 0.20*	< 0.005
Relative wall thickness	0.28 ± 0.06	0.30 ± 0.08	0.30 ± 0.07	0.31 ± 0.11	0.15
Cross-sectional area (mm^2)	16.64 ± 5.41	17.20 ± 5.44	19.65 ± 5.88	22.10 ± 5.71*†	< 0.0005
Plaque (%)	21	31	44*	56*	< 0.005

*$p < 0.05$ versus normal geometry. †$p < 0.05$ versus concentric remodeling. Data are presented as mean value ± SD or percent of patients.

in the present study are that hypertensive patients with concentric left ventricular hypertrophy have a greater increase in arterial wall thickness, cross-sectional area and stiffness at the operating level of distending pressure than hypertensive patients with other left ventricular geometric patterns, despite similarities between the groups in age, gender distribution and body size.

The concentration of arterial abnormalities in patients with concentric left ventricular hypertrophy is particularly notable because our patients with eccentric hypertrophy had equivalent blood pressures. Although there was a trend toward higher mean values of arterial wall thickness, diameter and cross-sectional area in the eccentric hypertrophy group, the values were statistically indistinguishable from those in patients with normal left ventricular geometry and concentric remodeling, despite considerably lower blood pressures in the latter two groups. The previous observation (3) that ambulatory pressures are highest in patients with concentric hypertrophy and are similar in groups with eccentric hypertrophy and concentric

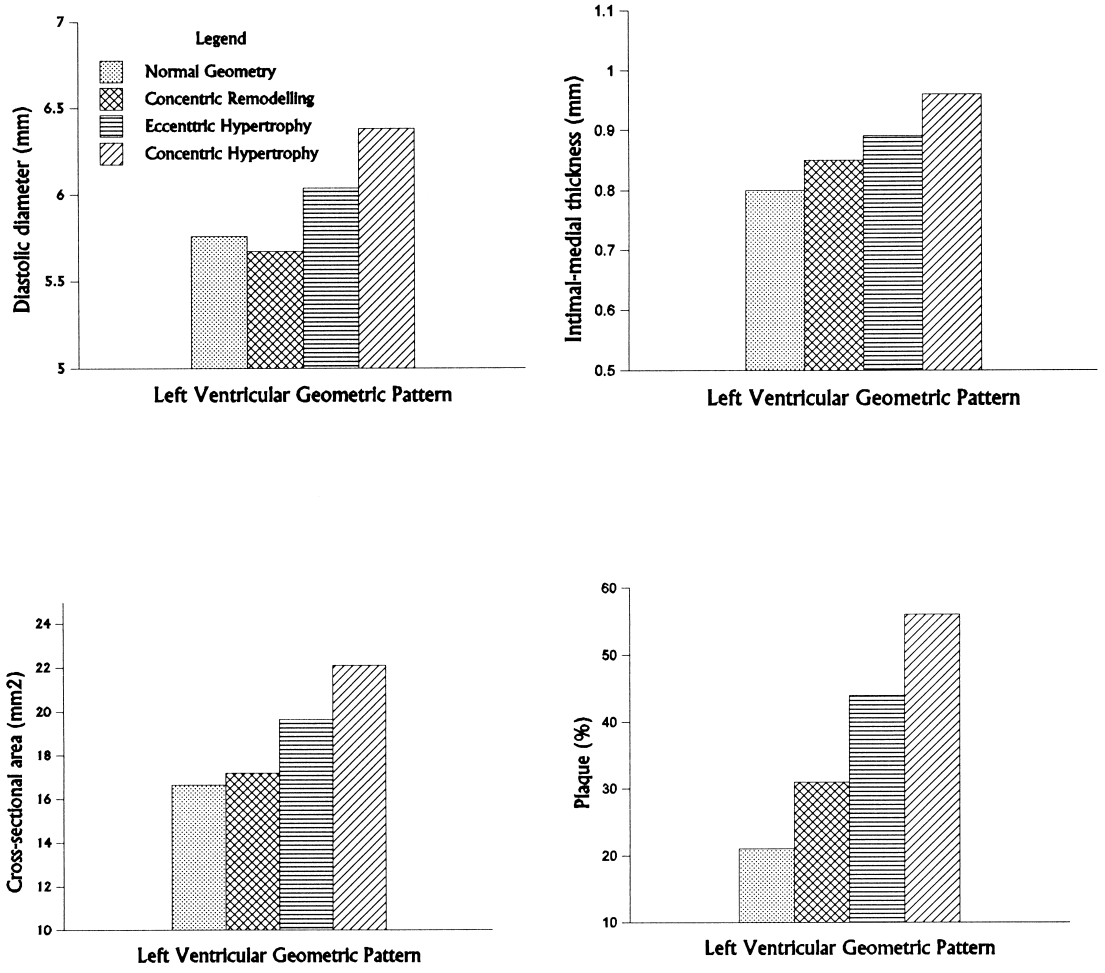

Figure 1. Relation of left ventricular geometric pattern to common carotid artery structure and prevalence of atherosclerosis.

Table 4. Carotid Artery Function

Variable	Normal Geometry (n = 176)	Concentric Remodeling (n = 54)	Eccentric Hypertrophy (n = 25)	Concentric Hypertrophy (n = 16)	Overall p Value
Vascular strain (%)	12.4 ± 3.7	12.0 ± 4.7	10.8 ± 3.8	9.5 ± 2.2*	< 0.005
Elastic modulus (dynes/cm^2 * 10^{-6})	471 ± 241	558 ± 263	614 ± 257	713 ± 265*	< 0.0005
Young's modulus (dynes/cm^2 per mm * 10^{-6})	601 ± 296	699 ± 373	683 ± 262	777 ± 219	< 0.05
Stiffness index (β)	5.79 ± 3.44	6.75 ± 3.23	6.80 ± 3.55	6.38 ± 1.40	0.08

*$p < 0.05$ versus normal geometry. Data are presented as mean value ± SD.

remodeling may provide an explanation for these results. However, among the 173 patients in the current study group who had ambulatory blood pressure monitoring, awake systolic but not diastolic pressures were significantly increased in both the concentric and eccentric hypertrophy groups versus in those with normal geometry (164/101 and 160/96 mm Hg, respectively, vs. 146/92 mm Hg, $p < 0.05$, for systolic pressure).

Alternatively, nonhemodynamic stimuli may be important. Although it has recently been reported that the angiotensin I–converting enzyme *DD* genotype is associated with both an increase in common carotid artery intimal-medial thickness (35) and electrocardiographic evidence of left ventricular hypertrophy (36), it remains to be determined whether there is more likely to be underlying concentric ventricular hypertrophy. The tendency toward a racial difference between the groups also supports the possibility of a genetic contribution to the differences in arterial structure.

Left ventricular geometry and carotid atherosclerosis. The prevalence of plaque was highest in the group with concentric hypertrophy (56%), particularly in comparison with the normal geometry and concentric remodeling groups, despite similarity among groups in age, serum lipids and smoking history. In fact, the percentage of current or former smokers was nearly half as much in the concentric hypertrophy group, although the difference was not statistically significant by the chi-square test. The higher prevalence of plaque in both the concentric and eccentric hypertrophy groups is in keeping with our previous observation of an association between carotid atherosclerosis and increasing left ventricular mass index in both normotensive and hypertensive subjects (14). The explanation for the current finding, and dissociation from the other arterial structural findings, is uncertain but may be at least partially explained by higher levels of both distending pressure and pulsatile forces resulting in greater susceptibility to endothelial damage.

Left ventricular geometry and arterial function. Measures of arterial function generally tended to be more abnormal in hypertensive patients with other geometric adaptations than in those with normal left ventricular geometry, but these differences mostly did not attain statistical significance, possibly because of wide scatter in the data as well as the modest size of some subgroups. The elastic modulus, a measure of vascular stiffness at its operating level of distending pressure, was significantly elevated in the concentric hypertrophy group. This finding is comparable to the earlier observation of Boutouyrie et al. (37), that left ventricular mean wall thickness and mass/volume ratio were inversely related to carotid artery distensibility and compliance in a group of 86 hypertensive patients. Their study did not include measurement of wall thickness or isobaric measures of arterial function; thus, it is uncertain whether their findings are predominantly related to distending pressure, as would appear to be the case in our study group.

Left ventricular geometry and arteriolar disease. Our findings in the carotid artery, representative of the large conduit arteries, are complemented by recent findings in the arteriolar system. In a recent study (38) of 140 Japanese patients with essential hypertension, 57 (41%) of whom were studied on medications, the patients with concentric hypertrophy (n = 20 [14%]) had the highest prevalence of grade III or IV retinopathy (53%) compared with those with normal geometry (0%), concentric remodeling (0%) and eccentric hypertrophy (29%, $p < 0.05$ for all comparisons). Serum creatinine was likewise highest in the group with concentric hypertrophy. Left ventricular mass was the strongest multivariate predictor of fundoscopic grade and serum creatinine. These findings are similar to those in our earlier report of a subgroup of hypertensive patients characterized by increased left ventricular chamber function, more marked concentric left ventricular hypertrophy and greater degrees of fundoscopic abnormalities and proteinuria (39). In the present study of otherwise healthy hypertensive patients, we detected no differences in serum creatinine among the four groups and did not systematically acquire data on arteriolar disease.

Study limitations. The present study group consisted overwhelmingly of patients with relatively mild hypertension, reducing the proportion of patients with either concentric or eccentric left ventricular hypertrophy, in contrast to previous studies (1–3,5,6,33). Whether study of hypertensive patients with more pronounced elevations in blood pressure and increases in left ventricular mass or with symptoms of cardiovascular disease would yield similar or even more pronounced results is uncertain. It is also possible that studying larger populations would reveal significant abnormalities of arterial geometry and stiffness in patients with eccentric left ventricular hypertrophy.

Clinical implications. Ultrasound imaging of the left ventricle and the extracranial carotid arteries reveals that the spectrum of geometric patterns seen in the heart in hypertension is partially paralleled by structural and functional changes in the arterial tree. In particular, patients with concentric left

ventricular hypertrophy had the most marked degrees of arterial hypertrophy, the least arterial expansion and the greatest arterial stiffness at the operating level of blood pressure. These findings lend further support to the importance of left ventricular geometry as a marker of target-organ damage and a means of risk stratification.

We thank Mariane C. Spitzer, RDMS, for her expertise in performance of the ultrasound studies, and Virginia Burns for her assistance in preparation of the manuscript.

References

1. Ganau A, Devereux RB, Roman MJ, et al. Patterns of left ventricular hypertrophy and geometric remodelling in essential hypertension. J Am Coll Cardiol 1992;19:1550–8.
2. 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;114:345–52.
3. Devereux RB, James GD, Pickering TG. What is "normal" blood pressure? Comparison of ambulatory blood pressure level and variability in patients with normal or abnormal left ventricular geometry. Am J Hypertens 1993;6 Suppl:211S–215S.
4. Verdecchia P, Porcellati C, Zampi I, et al. Asymmetric left ventricular remodelling due to isolated septal thickening in patients with systemic hypertension and normal left ventricular masses. Am J Cardiol 1994;73:247–52.
5. de Simone G, Devereaux RB, Roman MJ, et al. Assessment of left ventricular function by the midwall fractional shortening/end-systolic stress relation in human hypertension. J Am Coll Cardiol 1994;23:1444–51.
6. de Simone G, Devereaux RB, Roman MJ, Alderman MH, Laragh JH. Relation of obesity and gender to left ventricular hypertrophy in normotensive and hypertensive adults. Hypertension 1994;23:600–6.
7. Verdecchia P, Schillaci G, Borgioni C, et al. Adverse prognostic significance of concentric remodeling of the left ventricle in hypertensive subjects with normal left ventricular mass. J Am Coll Cardiol 1995;25:871–8.
8. Ford LE. Heart size. Circ Res 1976;39:297–303.
9. Ganau A, Arru A, Saba PS, et al. Stroke volume and left heart anatomy in relation to plasma volume in essential hypertension. J Hypertens 1991;9 Suppl 6:S150–S151.
10. Roman MJ, Saba PS, Pini R, et al. Parallel cardiac and vascular adaptation in hypertension. Circulation 1992;86:1909–18.
11. Saba PS, Roman MJ, Pini R, Ganau A, Devereux RB. Relation of carotid pressure waveform to left ventricular anatomy in normotensive subjects. J Am Coll Cardiol 1993;22:1873–80.
12. Gariepy J, Massonneau M, Levenson J, Heudes D, Simon A. Evidence for in vivo carotid and femoral wall thickening in human hypertension. Hypertension 1993;22:111–8.
13. Girerd X, Mourad J-J, Copie X, et al. Noninvasive detection of increased vascular mass in untreated hypertensive patients. Am J Hypertens 1994;7: 1076–84.
14. Roman MJ, Pickering TG, Schwartz JE, Pini R, Devereaux RB. The association of carotid atherosclerosis and left ventricular hypertrophy. J Am Coll Cardiol 1995;25:83–90.
15. Bikkina M, Levy D, Evans JC, et al. Left ventricular mass and risk of stroke in an elderly cohort. JAMA 1994;272:33–6.
16. Aronow WS, Kronzon I, Schoenfeld MR. Left ventricular hypertrophy is more prevalent in patients with systemic hypertension with extracranial carotid arterial disease than in patients with systemic hypertension without extracranial carotid arterial disease. Am J Cardiol 1995;76:192–3.
17. Schnall PL, Schwartz JE, Landsbergis PA, Warren K, Pickering TG. Relation between job strain, alcohol and ambulatory blood pressure. Hypertension 1992;19:488–94.
18. Devereux RB, Roman MJ. Evaluation of cardiac and vascular structure by echocardiography and other noninvasive techniques. In: Laragh JH, Brenner BM, eds. Hypertension: Pathophysiology, Diagnosis, Management. 2nd ed. New York: Raven Press, 1995:1969–85.
19. Devereux RB, Reichek N. Echocardiographic determination of left ventricular mass in man. Anatomic validation of the method. Circulation 1977;55: 613–8.
20. Devereux RB, Alonso DR, Lutas EM, et al. Echocardiographic assessment of left ventricular hypertrophy: comparison to necropsy findings. Am J Cardiol 1986;57:450–8.
21. Sahn DJ, DeMaria A, Kisslo J, Weyman A. Recommendations concerning quantitation in M-mode echocardiography: results of a survey of echocardiographic measurements. Circulation 1978;58:1072–83.
22. Schiller NB, Shah PM, Crawford M, et al. Recommendations for quantitation of the left ventricle by two-dimensional echocardiography. J Am Soc Echocardiogr 1989;2:358–67.
23. de Simone G, Devereux RB, Roman MJ, Schlussel Y, Alderman MH, Laragh JH. Echocardiographic left ventricular mass and electrolyte intake predict subsequent arterial hypertension in initially normotensive adults. Ann Intern Med 1991;114:202–9.
24. Ricotta JJ, Bryan FA, Bond MG, et al. Multicenter validation study of real-time (B-mode) ultrasound, arteriography, and pathologic examination. J Vasc Surg 1987;6:512–20.
25. Pignoli P, Tremoli F, Poli A, Oreste P, Paoletti R. Intimal plus medial thickness of the arterial wall: a direct measurement with ultrasound imaging. Circulation 1986;74:1399–1406.
26. Roman MJ, Pini R, Pickering TG, Devereux RB. Comparison of noninvasive measures of arterial compliance in normotensive and hypertensive patients. J Hypertens 1992;10 Suppl 6:S105–S108.
27. Kelly R, Hayward C, Ganis J, Daley J, Avolio A, O'Rourke M. Noninvasive registration of the arterial pressure waveform using high-fidelity applanation tonometry. J Vasc Med Biol 1989;1:142–9.
28. Kelly R, Fitchett D. The non-invasive determination of aortic input impedance and left ventricular power output. A validation and repeatability study of a new technique. J Am Coll Cardiol 1992;20:952–63.
29. Peterson LN, Jensen RE, Parnell R. Mechanical properties of arteries *in vivo*. Circ Res 1968;8:78–86.
30. O'Rourke M. Arterial stiffness, systolic blood pressure, and logical treatment of arterial hypertension. Hypertension 1990;15:339–47.
31. Hayashi K, Handa H, Nagasawa S, Okumura A, Moritaki K. Stiffness and elastic behavior of human intracranial and extracranial arteries. J Biomechanics 1980;13:175–84.
32. Hirai T, Sasayma S, Kawasaki T, Yagi S. Stiffness of systemic arteries in patients with myocardial infarction. A noninvasive method to predict severity of coronary atherosclerosis. Circulation 1989;80:78–86.
33. Mensah GA, Pappas TW, Koren MJ, Ulin RJ, Laragh JH, Devereux RB. Comparison of classification of hypertension severity by blood pressure level and World Health Organization criteria for prediction of concurrent cardiac abnormalities and subsequent complications in essential hypertension. J Hypertens 1993;11:1429–40.
34. Devereux RB. Left ventricular geometry, pathophysiology and prognosis. J Am Coll Cardiol 1995;25:885–7.
35. Castellano M, Muiesan ML, Rizzoni D, et al. Angiotensin-converting enzyme *I/D* polymorphism and arterial wall thickness in a general population: the Vobarno Study. Circulation 1995;91:2721–4.
36. Schunkert H, Hense H-W, Holmer SR, et al. Association between a deletion polymorphism of the angiotensin-converting enzyme gene and left ventricular hypertrophy. N Engl J Med 1994;330:1634–8.
37. Boutouyrie P, Laurent S, Girerd X, et al. Common carotid artery stiffness and patterns of left ventricular hypertrophy in hypertensive patients. Hypertension 1995;25(Pt 1):651–9.
38. Shigematsu Y, Hamada M, Mukai M, Mutsuoka H, Sumimoto T, Hiwada K. Clinical evidence for an association between left ventricular geometric adaptation and extracardiac target organ damage in essential hypertension. J Hypertens 1995;13:155–60.
39. Blake J, Devereux RB, Herrold EM, et al. Relation of concentric left ventricular hypertrophy and extracardiac target organ damage to supranormal left ventricular performance in established essential hypertension. Am J Cardiol 1988;62:246–52.