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Intima-media thickness evaluation by B-mode ultrasound. Correlation with blood pressure levels and cardiac structures

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Abstract

The aim of this study was to analyze the thickness of the intima-media complex (IMC) using a noninvasive method. The carotid and femoral common arteries were evaluated by noninvasive B-mode ultrasound in 63 normotensive and in 52 hypertensive subjects and the thickness of the IMC was tested for correlation with blood pressure, cardiac structures and several clinical and biological parameters. The IMC was thicker in hypertensive than in normotensive subjects (0.67 ± 0.13 and 0.62 ± 0.16 *vs* 0.54 ± 0.09 and 0.52 ± 0.11 mm, respectively, $P<0.0001$). In normotensive patients, the simple linear regression showed significant correlations between IMC and age, body mass index and 24-h systolic blood pressure for both the carotid and femoral arteries. In hypertensives the carotid IMC was correlated with age and 24-h systolic blood pressure while femoral IMC was correlated only with 24-h diastolic blood pressure. Forward stepwise regression showed that age, body mass index and 24-h systolic blood pressure influenced the carotid IMC relationship ($r^2 = 0.39$) in normotensives. On the other hand, the femoral IMC relationship was influenced by 24-h systolic blood pressure and age ($r^2 = 0.40$). In hypertensives, age and 24-h systolic blood pressure were the most important determinants of carotid IMC ($r^2 = 0.37$), while femoral IMC was influenced only by 24-h diastolic blood pressure ($r^2 = 0.10$). There was an association between carotid IMC and echocardiographic findings in normotensives, while in hypertensives only the left posterior wall and interventricular septum were associated with femoral IMC. We conclude that age and blood pressure influence the intima-media thickness, while echocardiographic changes are associated with the IMC.

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Key words
- Arterial thickness
- B-mode ultrasound
- 24-ABPM
- Cardiac structures

Introduction

After the validation of a noninvasive technique by Pignoli et al. (1) using ultrasound, several studies have been performed to analyze vascular changes in the presence of hypertensive (HT) disease. Most of these studies have demonstrated that vascular wall thickness, represented as intima-media complex (IMC), is thicker in large vessels such as the carotid and femoral arteries in hypertensive patients when compared to normotensive subjects (2,3). The physiopathological importance of wall thickening is probably as an adaptive mechanism in the early stages of hypertension to counterbalance the persistent increases in blood pressure levels. The vascular wall changes (hypertrophy/hyperplasia and remodeling) have been considered to be a hallmark of hypertensive disease in resistance vessels. In addition, the involvement of large vessels has been described as an early index of atherosclerosis (1). Furthermore, these arterial wall modifications occur in different segments of the arterial tree and represent an early involvement of the target organs due to hypertension. Some studies have demonstrated that 24-h ambulatory blood pressure measurement (ABPM) is more closely related to target organ damage than random measurements. These findings are more representative when we consider mean 24-h or daytime values (4-7). Blood pressure variability may be related to the severity of the damage of hypertensive target organ regardless of the levels of blood pressure (8). Cardiac structures assessed by echocardiography such as left ventricular mass index (LVMI), left ventricular mass (LVM) or the relative left ventricular posterior wall thickness (RPWT) and interventricular septum (RIVS) have shown good correlations with 24-h systolic blood pressure (24 h SBP) (9,10). In addition, it has been described that cardiovascular morbidity is associated in a parallel model not only with blood pressure levels but also with vascular structures (11,12). Several studies have reported that carotid wall changes may be related to other risk factors such as age, smoking and lipid levels (2,12-17). On the other hand, fewer studies relating femoral wall properties to age and blood pressure are available (2,3,13). In view of these considerations, the purpose of this study was to evaluate the structural changes of large vessels such as the common carotid and femoral arteries during the process of hypertension and aging, and to determine if these vascular modifications are related to cardiac structure findings.

Material and Methods

Sixty-three normotensive control subjects (32 men and 31 women aged 20-74 years) and 52 hypertensive patients (25 men and 27 women aged 23-72 years) were admitted to the study protocol after giving informed written consent. We defined normotension as the mean of three blood pressure measurements lower than 140/90 mmHg at the office and more than 50% of the valid measurements during 24-h monitoring lower than 140/90 mmHg (daytime) and 120/80 mmHg (nighttime). Hypertension was defined as blood pressure levels higher than 140/90 mmHg in at least three consecutive measurements and on three different occasions and more than 50% of valid measurements during ABPM higher than 140/90 mmHg (daytime) and 120/80 mmHg (nighttime), except for those who were on medication and had eventually normal blood pressure (Table 1). Twenty-five hypertensive patients (48%) were on medication and 16 (31%) had not been taking drugs for 8.3 ± 7.3 months (15 days-21 months); the remaining patients were newly diagnosed. Body mass index (BMI) was evaluated and overweight was defined as indexes above 25 kg/m^2 for women and 27 kg/m^2 for men. Smoking was defined as the absence (no) or presence (yes) of the habit regardless of the amount of cigarettes smoked

(packs/year). Participants who showed abnormal glucose levels (>140 mg/dl) as well as those with previous abnormalities upon echocardiographic evaluation or with previous heart disease were excluded. None of the participants showed hypertensive complications or peripheral arterial disease by clinical and biochemical assessment. The University Ethics Committee of UNIFESP approved this protocol.

Blood pressure determinations

Office blood pressure. Blood pressure levels were determined by the same physician with the patient in the seated position after 10 min at rest, using a mercury sphygmomanometer. SBP and diastolic blood pressure (DBP) corresponded to phases I and V of the Korotkoff sound, respectively, and the mean of three measurements was used in the analysis.

Blood pressure monitoring. Twenty-four-hour monitoring was performed using a non-invasive automatic monitor (SpaceLabs, model 90207, Redmond, WA, USA). Measurements were transmitted to an analytic system SpaceLabs ABP model 90209 (Data Interface Unit). We considered as daytime the period during which subjects performed their normal activities and nighttime as time slept. None of our subjects worked at night. Blood pressure was measured every 15 min during the daytime and every 20 min at night. Subjects who showed less than 80% valid measurements were excluded. The measurements of SBP and DBP obtained from this evaluation were used in the subsequent analysis of each period (24-h mean, daytime and nighttime). All participants were allowed to perform their normal daily activities and asked to write down any symptom in a diary. The cuff was positioned in the nondominant arm and was adjusted to the arm circumference. Levels lower than 70 mmHg or higher than 285 mmHg for systolic pressure and lower than 40 mmHg or higher than 200 mmHg for diastolic pressure were not considered. The cut-off values for daytime and nighttime were 140/90 mmHg and 120/80 mmHg, respectively.

Echocardiography. Cardiac structures were evaluated by M-mode and two-dimensional echocardiography (Esaote Biomédica, Florence, Italy) using a model SIM 5000 instrument equipped with a 2.5-MHz mechanical transducer. Patients assumed left decubitus with a slight rotation of the chest. The echocardiographic parameters evaluated were: left ventricular posterior wall thickness (PWT), interventricular septum thickness (IVS) both measured at diastole, LVM calculated according to the American Society of Echocardiography (18), using the cube-function formula: $LVM = 0.8\ [1.04\ (IVS + LVID + PWT)^3] - LVID^3)] + 0.6$ g, where LVID was the internal diameter of the left ventricle. LVMI was obtained by a division of LMV/body surface area and was considered to be normal when the values were below 110 g/m^2 for women and 134 g/m^2 for men. RPWT and RIVS were calculated according to RIVS = 2IVS/LVID and RPWT = 2PWT/LVID. Values below 0.45 were considered normal.

Biochemical parameters. All patients had blood samples drawn to determine lipid, glucose, creatinine, potassium, sodium and uric acid levels.

Arterial measurements. IMC was ultrasonographically evaluated (Ultramark 9-HDI-ATL; Bothel, WA, USA) with a 10.0-5.0-MHz linear broadband transducer. Both common carotid (CC-IMC) and common femoral (CF-IMC) posterior wall thicknesses were measured on the right side and at a distance of 2.0-3.0 cm proximal to the arterial bifurcation. A manual reading with a cursor was the method applied to measure IMC. All patients were submitted to at least two measurements of each artery by two different physicians in a blinded fashion and the mean of these values was used in the analysis. The intima-media image was analyzed at

telediastole to avoid variability in the measurements. Scanning of both arteries was performed in anteroposterior projections and to obtain a better image the sound beam was adjusted perpendicularly to the arterial surface of the posterior wall of the vessel, yielding two parallel lines which correspond to lumen-intima and intima-adventitia interfaces (IMC). All participants were in the supine position during the examination and were asked to perform a slight hyperextension of the neck for carotid measurement and a slight external rotation of the lower limb for femoral analysis. The reproducibility of IMC measurements was calculated as the standard deviation of the mean difference divided by the absolute mean of the measurements multiplied by 100, as described in the literature (19). The coefficient of variability was 12% for the carotid artery and 12.7% for the femoral artery, values that are within the normal range (20). The repeatability coefficient as defined by the British Standards Institution (21), which represents the estimated difference between two repeated measurements, was 10%. The overall absolute difference of repeated measurements for both CC-IMC and CF-IMC was 0.08 mm, lower than that described in the literature, which ranges from 0.1-0.15 mm (20).

Table 1 - Clinical parameters of the study groups.

Values are reported as mean ± SD or percentage of subjects. *P<0.001 *vs* normotensives; $^{+}$P<0.0001 *vs* normotensives (Student *t*-test). **P<0.05 *vs* normotensives; $^{++}$P<0.05 *vs* normotensives (Student *t*-test).

Parameter	Normotensive subjects (N = 63)	Hypertensive patients (N = 52)
Gender (M/F)	32/31	25/27
Age (years)	42 ± 13	51 ± 13*
BMI (kg/m^2)	25.7 ± 3.8	26.6 ± 3.8
Smoking (%)		
Yes	33.3	34.6
No	66.7	65.4
Blood pressure (mmHg)		
Office	116 ± 10/78 ± 6	149 ± 17/97 ± 8^{+}
24-h	118 ± 8/74 ± 6	141 ± 14/90 ± 9^{+}
Glucose (mg/dl)	86 ± 9.9	93 ± 12^{++}
Total cholesterol (mg/dl)	196 ± 36	213 ± 53**
LDL cholesterol (mg/dl)	127 ± 33	139 ± 45
HDL cholesterol (mg/dl)	51 ± 38	45 ± 14
Triglycerides (mg/dl)	116 ± 56	141 ± 81

Data analysis

Data were stored and analyzed with the SigmaStat for Windows software version 1.0 (Jandel Corporation, Chicago, IL, USA). The data are reported as means ± SD or medians and confidence intervals and were compared by the Student *t*-test. The relationship between continuous variables was evaluated by simple linear regression. Forward stepwise regression analysis was used in order to select the variables that might show a relative importance and might be predictors or potential determinants of changes in vascular structure. Differences were considered significant at P<0.05. The association between cardiac and vascular structures was determined by the Spearman correlation.

Results

Demographic data

As shown in Table 1, HT patients were older than normotensive control subjects (C) (P<0.001). There were no statistical differences in gender, body mass index or distribution of smokers between groups. Eighty-six percent of hypertensive patients reported a family history of hypertension, as opposed to 62% of the normotensive subjects.

Blood pressure levels measured at the office or by 24-h ambulatory monitoring were significantly higher in hypertensives when compared to controls (P<0.0001), as shown in Table 1. By comparing 24-h ABPM and casual values for each group, the C group showed a lower daytime systolic blood pressure (118 ± 8 *vs* 116 ± 10 mmHg, P<0.005) than that obtained at the office, and the HT group had a higher average of daytime diastolic blood pressure in relation

to casual diastolic blood pressure (92 ± 9 *vs* 97 ± 8 mmHg, P = 0.006).

All the structural echocardiographic variables analyzed in the hypertensive subjects showed higher values than in normotensive subjects, as shown in Table 2. In the control group only one subject (1.6%) showed both IVS and PWT above the normal range (12 mm). Although the median value for the hypertensive group was within the normal range, it was significantly higher than in normotensives. In 29% of the hypertensives IVS and PWT were above the normal range, and 19% showed left ventricular hypertrophy when adjusted for gender. Table 2 shows that common carotid and femoral walls were thicker in hypertensive patients when compared to controls.

No differences were found between men and women in either groups regarding age (41 ± 13 *vs* 43 ± 14 years), BMI (25.5 ± 2.9 *vs* 26.2 ± 5.2 kg/m^2), CC-IMC (0.55 ± 0.09 *vs* 0.53 ± 0.10 mm) and CF-IMC (0.54 ± 0.11 *vs* 0.50 ± 0.11 mm). No differences between treated and untreated patients in the HT group were observed when age (51 ± 13.3 *vs* 50 ± 13.1 years, ns), CC-IMC (0.67 ± 0.12 *vs* 0.67 ± 0.13 mm) and CF-IMC (0.66 ± 0.16 *vs* 0.64 ± 0.17 mm, respectively) were compared. The CC-IMC and CF-IMC were 24% and 19% thicker in hypertensives than in normotensives, respectively, although there was no difference between treated and untreated patients.

No differences in IMC for either artery were observed between smokers and nonsmokers. However, when we compared only nonsmokers in both groups, we observed a statistically significant difference (0.55 ± 0.10 *vs* 0.66 ± 0.12 mm for CC-IMC, P<0.0001, and 0.52 ± 0.11 *vs* 0.61 ± 0.14 mm for CF-IMC, P<0.002, C *vs* HT, respectively). Among smokers we also detected a significant difference between normotensive and hypertensive subjects (0.53 ± 0.08 *vs* 0.68 ± 0.15, P = 0.0007 for CC-IMC, and 0.51 ± 0.12 *vs* 0.71 ± 0.20 for CF-IMC, P<0.002, C and HT, respectively). These data suggest that smoking was not a limiting factor in our population, but the impact of high blood pressure was the major factor in the increase of IMC.

By using a simple linear regression model, we detected a positive correlation between CC-IMC and age in both groups (C: r = 0.49; HT: r = 0.53, P<0.0001, respectively) (Figure 1). Age was also positively related to CF-IMC in the C group (r = 0.44, P<0.0005) but not in hypertensives (r = 0.18, ns) (Figure 2). Only BMI correlated positive with CC-IMC and CF-IMC in the normotensive group (r = 0.43, P = 0.0005; r = 0.27, P<0.05, respectively). Conversely, none of

Table 2 - Vascular and cardiac parameters.

Cardiac structures are reported as median (confidence interval). Vascular IMC are reported as mean ± SD. *P<0.0001 *vs* normotensive subjects. IVS, Interventricular septum thickness; PWT, posterior wall thickness; LVM, left ventricular mass; LVMI, left ventricular mass index; RIVS, relative interventricular septum; RPWT, relative posterior wall thickness; ICM, intima-media complex.

Parameter	Normotensive subjects (N = 63)	Hypertensive patients (N = 52)
IVS (mm)	9 (7-10)	10 (9-12)*
PWT (mm)	9 (7-9)	10 (9-12)*
LVM (g)	132 (112-168)	175 (132-206)*
LVMI (g/m^2)	77 (66.5-91.8)	102 (85-116.8)*
RIVS	0.38 (0.32-0.40)	0.46 (0.39-0.52)*
RPWT	0.35 (0.32-0.38)	0.44 (0.39-0.51)*
Carotid IMC (mm)	0.54 ± 0.09	0.67 ± 0.13*
Femoral IMC (mm)	0.52 ± 0.11	0.62 ± 0.16*

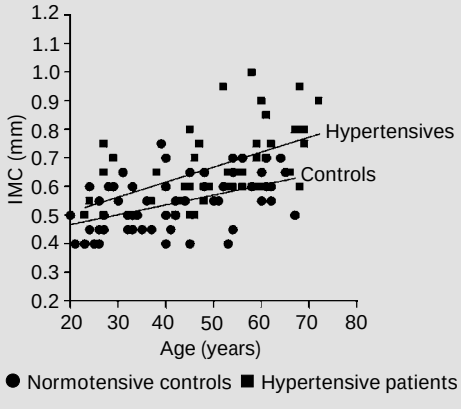

Figure 1 - Correlation between common carotid intima-media complex (IMC) and age for normotensive controls (N = 63) and hypertensive patients (N = 52). The equation for IMC-normotensives was: y = 0.398 + (0.0034 x age) and for IMC-hypertensives: y = 0.405 + (0.0052 x age). The intercepts, but not the slopes, were different.

the clinical or biological parameters studied correlated with arterial structures of the hypertensive group.

Neither systolic nor diastolic BP values obtained at the office were correlated with CC-IMC in the C or in the HT group. On the other hand, a positive correlation of CF-IMC with systolic (r = 0.43, P<0.0005) and diastolic (r = 0.43, P<0.005) blood pressure values was observed in normotensive subjects. Analysis of the 24-h ABPM showed that CC-IMC was positively correlated with 24-h SBP in control (r = 0.34, P = 0.007) as well as in hypertensive subjects (r = 0.45, P<0.005) (Figure 3). CF-IMC showed a positive and stronger correlation with 24-h SBP (r = 0.50, P<0.0001) than with 24-h DBP (r = 0.36, P<0.005) in normotensives. In the hypertensive group, only 24-h DBP was correlated with CF-IMC (r = 0.32, P<0.05) (Figure 4). Only triglycerides were correlated with CF-IMC (r = 0.50, P<0.0001) in the control group.

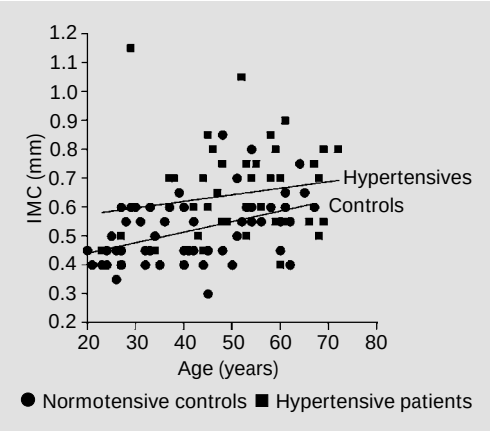

Figure 2 - Correlation between common femural intima-media complex (IMC) and age for normotensive controls (N = 63) and hypertensive patients (N = 52). The equation for IMC-normotensives was: y = 0.367 + (0.0036 x age) and for IMC-hypertensives: y = 0.529 + (0.0023 x age). The intercepts, but not the slopes, were different.

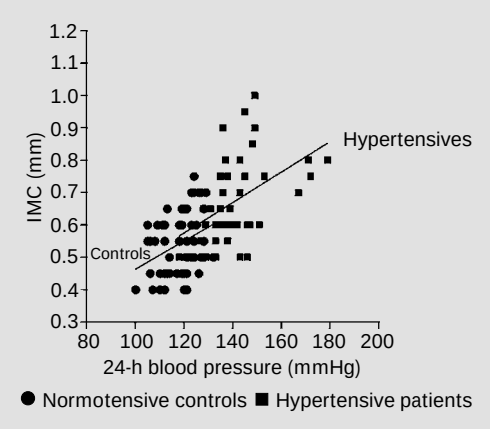

Figure 3 - Correlation between common carotid intima-media complex (IMC) and 24-h SBP for normotensive controls (N = 63) and hypertensive patients (N = 52). The equation for IMC-normotensives was: y = 0.028 + (0.0043 x 24-h SBP) and for IMC-hypertensives: y = 0.0093 + (0.0047 x 24-h SBP).

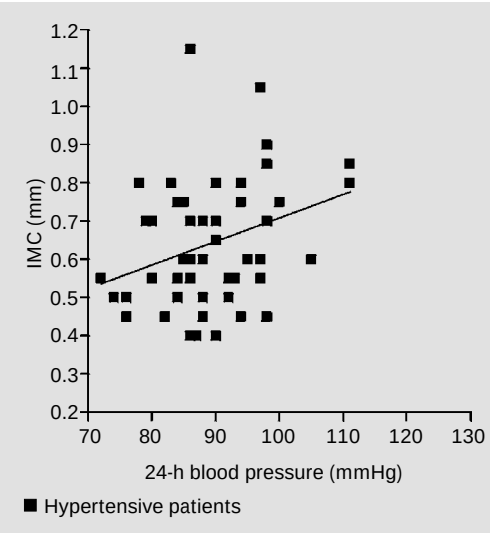

Figure 4 - Correlation between common femural intima-media complex (IMC) and 24-h DBP. Hypertensive patients (N = 52). The equation for IMC-hypertensives was: y = 0.09 + (0.0062 x 24-h DBP).

Forward stepwise regression was performed to determine which variables might be independently related to vascular structural changes and be considered as predictors of arterial wall thickness. Tables 3 and 4 summarize these results. In both groups, age was the most powerful predictor of common carotid thickening. Other factors related to carotid IMC in the normotensive group were BMI and 24-h SBP. In hypertensives, in addition to age, 24-h SBP was independently related to the increased wall thickness. Twenty-four-hour SBP and age predicted CF-IMC in the control group, while only 24-h DBP did so in the hypertensive group. Other clinical or biological parameters such as gender, body mass index, smoking and family history of hypertension were not entered in the regression model.

Most of the structural echocardiographic variables were associated with arterial wall changes. Thus, in the normotensive group absolute IVS, absolute and relative PWT and LVMI were associated with both carotid and femoral IMC. In hypertensives, CC-IMC was not associated with cardiac structures except for relative IVS; CF-IMC showed a strong association with absolute and relative IVS and PWT in this group, as shown in Table 5.

Discussion

In the present study, we observed that both common carotid and femoral wall thickness were more increased in hypertensives when compared to normotensives, which is in accordance to several previous studies (2,3,14,17). The fact that hypertensive patients were older than normotensives did not alter the expectation that hypertension may affect arterial walls, as demonstrated by the remaining differences in the thickness of both arteries when the groups were matched by age (carotid: 0.56 ± 0.10 *vs* 0.67 ± 0.13 mm, P<0.0001; femoral: 0.54 ± 0.12 *vs* 0.64 ± 0.17 mm, P<0.005). From a general point of view, our data demonstrate that structural wall changes detected in each arterial segment were influenced by age and blood pressure levels, although with different intensities for each artery.

CC-IMC determinants and their relation to cardiac structures

Most studies have suggested that age is the strongest determinant of carotid wall thickening, and systolic blood pressure has been considered as the secondary determinant in hypertensive and normotensive subjects (2,16,17,22,23). The impact of blood pressure levels in hypertensives has been considered as an accelerated form of aging. However, when we analyzed both groups matched for age, hypertensives had a 12% thicker CC-IMC at age forty, and 21% at age sixty when compared to normotensives. Therefore, this analysis shows that, for the same arterial wall thickness, the thickness of the arterial wall in a hypertensive subject seems to be similar to that found in a normotensive subject 20 years older. Therefore, our hypothesis is that hypertensive patients develop an aging process in their arterial wall earlier in life.

Other factors found to contribute to CC-IMC thickness in our normotensives were BMI and, to a lesser extent, 24-h SBP. The role of BMI in arterial wall thickening is poorly understood and its influence is probably independent of age, since we did not find any correlation between them. In our hypertensives, BMI had no impact on arterial wall thickening, as shown by forward stepwise regression and by association analysis for both carotid and femoral arteries. With respect to this particular issue, we may

Table 3 - Results of forward stepwise multiple regression of factors influencing common carotid (CC)- and common femural (CF)-intima-media complex (IMC) in normotensive controls (N = 63).

BMI, Body mass index; SBP, systolic blood pressure.

Dependent variable: CC-IMC Multiple R = 0.39				
Variable	Coefficient	Standard error	Multiple R	P
Constant	-0.0848	0.1574		
Age	0.00271	0.000747	0.224	0.0006
BMI	0.00730	0.00274	0.117	0.0099
24-h SBP	0.00273	0.00135	0.045	0.048
Dependent variable: CF-IMC Multiple R = 0.40				
Variable	Coefficient	Standard error	Multiple R	P
Constant	-0.427	0.1822		
24-h SBP	0.00686	0.0015	0.247	<0.0001
Age	0.00324	0.00086	0.151	0.0002

Table 4 - Results of forward stepwise multiple regression of factors influencing common carotid (CC)- and common femural (CF)-intima-media complex (IMC) in hypertensive patients (N = 52).

SBP, Systolic blood pressure; DBP, diastolic blood pressure.

Dependent variable: CC-IMC Multiple R = 0.37				
Variable	Coefficient	Standard error	Multiple R	P
Constant	0.02601	0.173		
Age	0.0428	0.00125	0.291	0.0013
24-h SBP	0.00306	0.00132	0.074	0.02
Dependent variable: CF-IMC Multiple R = 0.10				
Variable	Coefficient	Standard error	Multiple R	P
Constant	0.0913	0.241		
24-h DBP	0.00616	0.0027	0.101	0.03

speculate that hypertension overwhelms other factors such as BMI and age.

The impact of blood pressure levels, on the other hand, may be explained as a response to the tension applied on the wall. Some experimental data obtained for 1-day-old *SHR* rats with nonsustained hypertension revealed that the media layer of the carotid artery was thicker when compared to Wistar-Kyoto rats at the same age, suggesting that this change occurs prior to the development of hypertension and could be considered as a primary damage (24).

Regarding the viscoelastic properties of carotid vessels, some data have shown that distensibility is lower even in borderline hypertensive patients when compared to normotensives. The carotid artery becomes stiffer with age, reaching lower distensibility levels than those observed in the femoral artery at an early age (25,26).

In relation to cardiac structures, the C group showed positive associations between CC-IMC and all cardiac parameters analyzed, especially left ventricular mass. Also, as previously described, CC-IMC was correlated with SBP. Thus, we may speculate that SBP similarly causes structural changes in the vessel walls and in the heart. It is also likely that age can play a role both in vessels and in the heart in a parallel fashion. Contrasting with the reports available in the literature, there was no association between vascular and cardiac structural changes in our hypertensive patients (11,12,27). This may be explained by the impact of the antihypertensive treatment, taken by most of our patients, which may mask the changes in cardiac structures.

A recent analysis concerning carotid artery wall and left ventricular mass showed that the cross-sectional IMC area may be an independent indicator of left ventricular mass. It is not valid for IMC, even in patients within the normal range (28).

Table 5 - Spearman correlation coefficient between common carotid (CC)- and common femural (CF)-intima-media complex (IMC) and cardiac parameters in control and hypertensive groups.

For abbreviations see legend to Table 2. NS, Non-significant.

Group	CC-IMC		CF-IMC	
	r	P	r	P
Control				
IVS (mm)	0.36	0.006	0.32	0.02
PWT (mm)	0.41	0.002	0.36	0.007
LVM (g)	0.43	0.0001	0.33	0.01
LVMI (g/m^2)	0.29	0.03	0.31	0.02
RIVS	0.23	NS	0.25	NS
RPWT	0.30	0.02	0.30	0.02
Hypertensive				
IVS (mm)	0.27	NS	0.42	0.003
PWT (mm)	0.18	NS	0.37	0.009
LVM (g)	0.12	NS	0.16	NS
LVMI (g/m^2)	0.14	NS	0.21	NS
RIVS	0.30	0.04	0.45	0.001
RPWT	0.24	NS	0.40	0.005

CF-IMC determinants and their relation to cardiac structures

Few studies of the properties of the femoral artery have been conducted in humans. A previous study comparing different segments of the arterial tree obtained at autopsy showed that relative stiffness was most marked in the femoral artery, particularly in young subjects (29). Our data showed that 24-h SBP and age influenced the wall thickening in normotensive controls, although to a lesser extent than in hypertensives. Conversely, in hypertensive patients femoral wall thickening was correlated only with 24-h DPB. This contrasts with some reports in the literature, in which age was found to be positively correlated with CF-IMC in both normotensive and hypertensive subjects (2). This discrepancy may be due to the treatment that our patients underwent during the study. However, Benetos et al. (13) have reported that the femoral artery is less compliant than the carotid artery and is not affected by aging or high blood pressure, in partial agreement with our findings.

An interesting aspect of our analysis is the fact that in the fourth decade of life CF-IMC was 25% thicker in hypertensives, but in the sixth decade the femoral wall was only 11% thicker than in normotensives. This response to aging and hypertension was opposite to that seen in the carotid wall, suggesting that the femoral artery reacts in a different way to high blood pressure and that an early degenerative process occurs in the femoral wall of hypertensive patients.

Kawasaki et al. (30) also demonstrated greater stiffness of the femoral artery with aging than of the proximal arteries. According to Armentano et al. (25), blood pressure causes changes in the geometric properties of the femoral artery due to an intrinsic dilation and loss of pulsatile distension. Under the influence of high blood pressure, our patients developed wall thickening as an adaptative process to maintain wall tension. As demonstrated by Armentano et al., once the degenerative process begins, it could be an adaptative process which does not allow progressive thickening of the femoral arteries. Besides, other factors may play a role in the femoral responses to hypertension and age, such as upright position, hydrostatic pressure, anatomic variations and higher susceptibility to cardiovascular risk factors.

We believe that the present study provides evidence that cardiac structural changes are correlated with femoral wall thickness and occur earlier than in the carotid artery. We suggest that the increase of both the posterior wall and the interventricular septum thickness precedes the development of left ventricular hypertrophy, and occurs in an early phase of heart damage in the hypertensive process. The association between cardiac and vascular structures found in our study, especially with respect to femoral wall thickness, might represent an amplifier mechanism for progressive elevation of blood pressure levels, which leads to more severe hypertension and heart damage.

In conclusion, our results show that the use of a noninvasive method such as B-mode ultrasound for the carotid and femoral arteries is reliable and helpful in evaluating hypertensive patients. Amongst the several factors which have an impact on target organs, age and high blood pressure levels appear to be the main predictors of increased thickening of the arterial wall.

References

1. Pignoli P, Tremoli E, Poli A, Oreste P & Paoletti R (1986). Intimal plus medial thickness of the arterial wall: a direct measurement with ultrasound imaging. *Circulation*, 74: 1399-1406.
2. Gariepy J, Massoneau M, Levenson J, Heudes D, Simon A & the Groupe de Prévention Cardio-vasculaire en Medicine du Travail (1993). Evidence for *in vivo* carotid and femoral wall thickening in human hypertension. *Hypertension*, 22: 111-118.
3. Eiskjær H, Christensen T & Pedersen EB (1989). Abnormal structure and increased stiffness on the femoral arterial wall in young patients with sustained essential hypertension. *Journal of Internal Medicine*, 226: 235-240.
4. Perloff D, Sokolow M & Cowan R (1983). The prognostic value of ambulatory blood pressures. *Journal of the American Medical Association*, 249: 2792-2798.
5. Hartford M, Wikstrand J, Wallentin I, Ljungman S & Berglund G (1983). The relation between cardiac hypertrophy and hypertension. *Acta Medica Scandinava*, 672 (Suppl): 101-104.
6. White WB, Schulman P, McCabe EJ & Dey HM (1989). Average daily blood pressure, not office blood pressure, determines cardiac function in patients with hypertension. *Journal of the American Medical Association*, 261: 873-877.
7. White WB (1991). Relationship among casual and ambulatory blood pressure and target organ involvement in essential hypertension. *Clinical and Investigative Medicine*, 14: 22-30.
8. Parati G, Pomidossi G, Albini F, Malaspina D & Mancia G (1987). Relationship of 24-h blood pressure mean and variability to severity of target-organ damage in hypertension. *Journal of Hypertension*, 5: 93-98.
9. Rowlands DB, Ireland MA, Glover DR, McLeay RAB, Stallard TJ & Littler WA (1981). The relationship between ambulatory blood pressure and echocardiographically assessed left ventricular hypertrophy. *Clinical Science*, 61 (Suppl 7): 101S-103S.
10. Devereux RB & Pickering TG (1990). Relationship between ambulatory or exercise blood pressure and left ventricular structure: prognostic implications. *Journal of Hypertension*, 8 (Suppl 6): S125-S134.
11. Devereux RB, Roman MJ, Ganau A, de Simone G, Okin PM & Klingfield P (1994). Cardiac and arterial hypertrophy and atherosclerosis in hypertension. Clinical Con-

ference. *Hypertension*, 23 (Part 1): 802-809.
12. Roman MJ, Saba PS, Pini R, Spitzer M, Pickering TG, Rosen S, Alderman MH & Devereux RB (1992). Parallel cardiac and vascular adaptation in hypertension. *Circulation*, 86: 1909-1918.
13. Benetos A, Laurent S, Hoecks AP, Boutouyrie PH & Safar ME (1993). Arterial alterations with aging and high blood pressure. A noninvasive study of carotid and femoral arteries. *Arteriosclerosis and Thrombosis*, 13: 90-97.
14. Lonatti L, Cuspidi C, Sampieri L, Boseli L, Bocciolone M, Leonetti G & Zanchetti A (1993). Ultrasonographic evaluation of cardiac and vascular changes in young borderline hypertensives. *Cardiology*, 83: 298-303.
15. Ludwig MM, Joeger U, Lund S & Stump KO (1993). Divergent responses of CC artery intimal-medial thickness to high blood pressure and hypercholesterolemia in relation to age. *Journal of Hypertension*, 11 (Suppl 5): S130-S131.
16. Muiesan ML, Pasini GF, Salvetti M, Calebich S, Zulli R, Castellano M, Rizzoni D, Bettoni G, Cinelli A, Porteri E, Corsetti V & Agabiti-Rosei E (1996). Cardiac and vascular structural changes. Prevalence and relation to ambulatory blood pressure in a middle-aged general population in Northern Italy: The Vobarno study. *Hypertension*, 27: 1046-1051.
17. Salonen R & Salonen JT (1991). Determinants of carotid intima-media thickness: a population-based ultrasonography study in Eastern Finnish man. *Journal of Internal Medicine*, 229: 225-231.
18. Sahn DJ, DeMaria A, Kisslo J & Weyman A (1978). The Committee on M-mode standardization of the American Society of Echocardiography. Recommendations regarding quantitation in M-mode echocardiography: results of a survey of echocardiographic measurements. *Circulation*, 58: 1072-1083.
19. Vannine E, Mustonen J, Vainio P, Lansimies E & Uusitupa M (1992). Left ventricular function and dimensions in newly diagnosed non-insulin dependent diabetes mellitus. *American Journal of Cardiology*, 70: 371-378.
20. Bruschi G, Cabassi A, Orlandini G, Regolisti G, Zambrelli P, Calzolari M & Borgheti A (1997). Use of Fourier shape descriptors to improve the reproducibility of echographic measurements of arterial intima-media thickness. *Journal of Hypertension*, 15: 467-474.
21. British Standards Institution (1979). *Precision of Test Methods*: *1. Guide for the Determination and Reproducibility for a Standard Test Method (BS 5497, Part 1)*. British Standards Institution, London.
22. Benetos A, Laurent S, Boutouyrie P & Safar M (1991). Alteration in the carotid artery wall properties with aging and high blood pressure level. *Journal of Hypertension*, 9 (Suppl 6): S112-S113.
23. Handa N, Matsumoto M, Maeda H, Hougaku H, Ogawa S, Fukunaga R, Yoneda S, Kimura K & Kamada T (1990). Ultrasonic evaluation of early carotid atherosclerosis. *Stroke*, 21: 1567-1572.
24. Gray SD (1982). Anatomical and physiological aspects of cardiovascular function in Wistar-Kyoto rats and spontaneously hypertensive rats. *Clinical Science*, 63: 3835-3855.
25. Armentano R, Megnien JL, Simon A, Bellenfant F, Barra J & Levenson J (1995). Effects of hypertension on viscoelasticity of carotid and femoral arteries in humans. *Hypertension*, 26: 48-54.
26. Reneman RS & Hoecks AP (1995). Arterial distensibility and compliance in hypertension. *Netherlands Journal of Medicine*, 47: 152-161.
27. Roman MJ, Pickering TG, Pini R, Schwartz JE & Devereux RB (1995). Prevalence and determinants of cardiac and vascular hypertrophy in hypertension. *Hypertension*, 26: 369-373.
28. Linhart A, Gariepy J, Giral P, Levenson J & Simon A (1996). Carotid artery and left ventricular structural relationship in asymptomatic men at risk for cardiovascular disease. *Atherosclerosis*, 127: 103-112.
29. Learoyd BM & Taylor MG (1966). Alterations with age in the viscoelastic properties of human arterial walls. *Circulation Research*, XVIII: 278-292.
30. Kawasaki T, Sasayama S, Yagi S-I, Asakawa T & Hirai T (1987). Non-invasive assessment of the age related changes in stiffness of major branches of the human arteries. *Cardiovascular Research*, 21: 678-687.