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The Relationship of Carotid Arterial Stiffness and Left Ventricular Concentric Hypertrophy in Hypertension

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A – research concept and design; **B** – collection and/or assembly of data; **C** – data analysis and interpretation; **D** – writing the article; **E** – critical revision of the article; **F** – final approval of article

Abstract

Background. Left ventricular hypertrophy (LVH) and geometry patterns vary in different hemodynamic profiles The concentric hypertrophy (CH) pattern has been proved to have the worst prognosis.
Objectives. The aim of the study was to test the hypothesis that carotid artery stiffness, as a marker of vascular damage, is associated with CH, independently of other potential determinants such as demographic factors (age, sex, BMI), clinical parameters (smoking, diabetes, creatinine level) and hemodynamic variables (blood pressure, pulse pressure [PP]).
Material and Methods. The study involved 262 subjects (89 men): 202 patients with hypertension (153 untreated, 49 on medication), aged 55.7 ± 10 years, and 60 age-matched normal controls. The subjects were examined by echocardiography and carotid ultrasound with a high-resolution echo-tracking system. Based on the left ventricular mass index (LVMI) and relative wall thickness (RWT), the patients with hypertension were divided into four patterns of LVH and geometry: normal geometry (N, n = 57), concentric remodeling (CR, n = 48), concentric hypertrophy CH (n = 62) and eccentric hypertrophy (EH, n = 35). Intima-media thickness (IMT) and the parameters of arterial stiffness were also assessed using the β stiffness index (β), Young elastic modulus (Ep), arterial compliance (AC), one-point pulse wave velocity (PWVβ) and the wave reflection augmentation index (AI).
Results. Univariate analysis showed that the following variables are significant in determining CH: β > 8.4, Ep > 136 kPa, PWVβ > 7.1 m/s, AI > 21.9%, systolic BP > 151 mm Hg, PP > 54, IMT > 0.56 and the presence of diabetes. However, by multivariate analysis only AI (OR 3.65, p = 0.003), PWVβ > 7.1 m/s (OR 2.86, p = 0.014), systolic BP (OR 3.12, p = 0037) and the presence of diabetes (OR 3.75, p = 0.007) were associated independently with the occurrence of CH.
Conclusions. Concentric hypertrophy in hypertension is strongly associated with carotid arterial stiffness and wave reflection parameters, independently of the influence of systolic blood pressure and diabetes (**Adv Clin Exp Med 2016, 25, 2, 263–272**).

Key words: hypertension, left ventricular concentric hypertrophy, arterial stiffness.

Assessment of both left ventricular hypertrophy (LVH) and abnormal structure and function of the conduit arteries as features of the target organ damage (TOD) is crucial in the risk stratification and management of patients with arterial hypertension [1]. It is still unclear how structural and functional arterial changes contribute to the pathophysiology of LVH. One concept is that arterial remodeling might parallel left ventricular (LV) remodeling due to pressure overload and additional non-hemodynamic factors in hypertension [2]. This phenomenon might have an impact on the in-

creased incidence of cardiovascular events in patients with LVH [3]. LVH and geometry patterns vary in different hemodynamic profiles, which has clinical and prognostic implications [4, 5]. The concentric hypertrophy (CH) pattern has been proved to have the worst prognosis [5, 6]. The relationship of CH and atherosclerotic changes of carotid arteries has already been established [7, 8].

Arterial stiffness may influence cardiac hypertrophy independently of the effects of blood pressure, but data are inconsistent. The detailed mechanisms by which arterial stiffness might be involved in cardiac geometric remodeling secondary to hypertension have not yet been established.

The standard recommended method for assessing arterial stiffness is the measurement of carotid-femoral pulse wave velocity (PWV), because it is simple, direct and reproducible [9, 10]. However, carotid-femoral PWV provides the average function of different segments of the aorta that may have very different elastic properties, so assessment of local arterial stiffness at specific sites is also of interest [10]. New high-resolution echo-tracking systems offer the possibility of complex ultrasound assessment of local arterial stiffness, wave reflection analysis parameters and intima-media thickness (IMT) in a simple procedure that can be conducted at the patient's bedside [11–13].

The aim of the study was to test the hypothesis that carotid arterial stiffness is associated with CH independently of IMT, demographic factors (age, sex, BMI), clinical parameters (cigarette smoking, diabetes, creatinine level) and hemodynamic variables (steady and pulsatile blood pressure components).

Material and Methods

The study involved 262 subjects (89 males and 173 females) recruited from two centers (the Department of Cardiology at T. Marciniak Lower Silesian Hospital in Wrocław, Poland, and the Carol Davila University of Medicine and Pharmacy in Bucharest, Romania) in 2005–2011. The subjects were divided into two groups: Group I: 202 patients with hypertension, mean age 55.7 ± 10.4 years. Group II: 60 healthy control subjects.

Hypertensives were defined as subjects with a history of hypertension (the mean duration of the disease was 2.7 years) in whom increases in blood pressure values (> 140 mm Hg systolic and/or > 90 mm Hg diastolic) were observed in at least three measurements performed on several different days. None of the patients exceeded grade I hypertension according to European Society of Cardiology guidelines [1]. Among the 202 hypertensives, 49 (24%) were being treated with antihypertensive drugs (ACE inhibitors 55%; angiotensin receptor blockers 12%, beta-blockers 45%, calcium channel blockers 33%, and diuretics 43%). Among the diabetics (n = 90), 74% were being treated by oral hypoglycemic agents; the mean value of HbA1c in the diabetes group was 7.3 ± 1.4 %. The control group consisted of healthy volunteers without cardiovascular risk, whose results were used to establish normal values of arterial stiffness parameters. All the participants were examined by a cardiologist with the use of an ECG and echocardiography. Only patients with preserved LV systolic function (EF > 55%) and without cardiomyopathy, pericardial disease and valve pathology were enrolled. Subjects with ischemic heart disease (defined as a history of angina and/or myocardial infarction, with Q waves on ECG and/or regional LV wall motion abnormalities on echocardiography) were excluded from this study.

All the patients underwent comprehensive clinical examination, ECG, echocardiography, vascular assessments and an evaluation of biological parameters.

The study protocol was approved by the local research ethics committees and informed consent was collected from all the subjects.

Echocardiography

All the patients were subjected to echocardiography using an Alpha 10 ultrasound (Hitachi-Aloka, Tokyo Japan) with an assessment of the LV geometry pattern as reported in a previous publication [13]. M-mode measurements of the end diastolic wall thickness (of the interventricular septum [IVS] and posterior wall [PW]) and the LV end-diastolic diameter (EDD) were entered into the formula by Devereux et al. [14] for the calculation of LV mass (LVM). LVM was indexed to body surface area (BSA), giving LV mass index (LVMI). Relative wall thickness (RWT) was assessed using the formula RWT = 2PW/EDD.

Left ventricular hypertrophy (LVH) was determined when LVMI was > 110 g/m^2 in women and > 125 g/m^2 in men [14]. Based on LVMI and RWT (treating 0.42 as a cut-off point), hypertensives were classified into four patterns of LVH and geometry [4]:

– normal geometry (N, n = 57), both LVMI and RWT within normal limits;

– concentric remodeling (CR, n = 48), normal LVMI with increased RWT (> 0.42);

– concentric hypertrophy (CH, n = 62), both LVMI and RWT increased;

– eccentric geometry (EH, n = 35), increased LVMI, normal RWT (≤ 0.42).

Integrated Assessment of Arterial Function

Vascular ultrasound of the right common carotid artery was performed as described in a previous publication [13], using an Alpha 10 ultrasound (Hitachi-Aloka, Tokyo, Japan) equipped with an integrated and automated ultrasound, Doppler and high resolution echo-tracking system. The following arterial stiffness parameters were evaluated [13, 15]:

- β: the beta stiffness index, calculated as the ratio of the natural logarithm of systolic/diastolic blood pressure to the relative change in artery diameter:

$$\beta = \ln (Ps/Pd)/[(Ds - Dd)/Dd],$$

where ln – the natural logarithm, Ps – systolic blood pressure, Pd – diastolic blood pressure, Ds – arterial systolic diameter and Dd – arterial diastolic diameter.

- Ep (epsilon): Young's modulus, also known as the pressure-strain elasticity modulus:

$$Ep = (Ps - Pd)/[(Ds - Dd)/Dd].$$

- AC: arterial compliance, determined from the arterial cross-sectional area and blood pressure:

$$AC = \pi(Ds \times Ds - Dd \times Dd)/ [4 \times (Ps - Pd)].$$

- PWVβ: one-point pulse wave velocity, calculated from the time delay between two adjacent distension waveforms, based on the water hammer equation and using the β stiffness index:

$$PWV\beta = \sqrt{\frac{\beta \cdot P}{2 \cdot \rho}},$$

where P – diastolic blood pressure and ρ – blood density (1050 kg/m^3).

- AI: augmentation index as a wave reflection parameter and a surrogate for arterial stiffness was determined as AI = ΔP/PP, and is illustrated in Fig. 1.

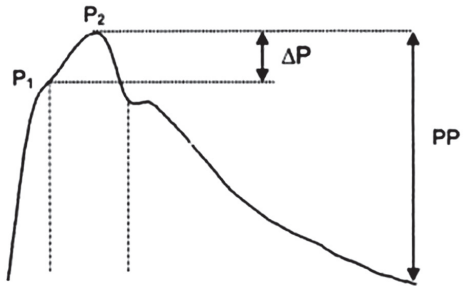

Fig. 1. The method of calculating the augmentation index, from Mancia et al. [1]; PP – pulse pressure; P_1 – first systolic peak; P_2 – second systolic peak; delta (Δ) P = $P_2 - P_1$

The reproducibility of these measurements was reported in a study by Sugawara et al. [16].

An original example of the examination of the arterial stiffness parameters derived from the right common carotid artery, using a high resolution echo-tracking system, is presented in Fig. 2.

Intima-media thickness (IMT) was measured according to the standards published by Magda et al. [17].

In addition, serum creatinine levels and lipids were measured in all the patients.

Statistical Analysis

Mean and standard deviations were calculated for quantitative variables, and percentages were calculated for qualitative variables. All quantitative variables that were not normally distributed, and differences between groups, were tested using the Mann-Whitney test and Kruskal-Wallis test; the χ^2 test was used to calculate the percentages of qualitative variables. Statistical significance was set at $p < 0.05$ in two-sided tests; in multiple testing statistical significance was set at $p < 0.01$. For quantitative variables with a statistically significant difference between the two groups, receiver-operating characteristic (ROC) curves were determined to calculate the cut-off values optimized to reach the best compromise in the prediction of concentric hypertrophy. Optimal cutoff was defined as the threshold where the sum of sensitivity and specificity was at the maximum.

The correlation analysis was performed using Spearman's rank correlation coefficient test. A multivariable logistic regression analysis was conducted considering the occurrence of concentric hypertrophy an dependent variable. All the variables that presented a significant value < 0.25 in the univariate analysis were included in the model. The stepwise forward method was used and odds ratios (OR) with 95% CI were calculated. The model was evaluated using the Hosmer-Lemeshow test.

Results

The characteristics of the study group are presented in Table 1.

There were no significant differences between the four patterns of LVH and geometry in terms of age, gender, obesity, heart rate, smoking, lipids, creatinine level and IMT.

BP parameters were the highest in the CH and CR groups. Systolic BP and PP were the highest in the CH group; diastolic BP was the highest in the CR group. Subjects with CH were more likely to have diabetes.

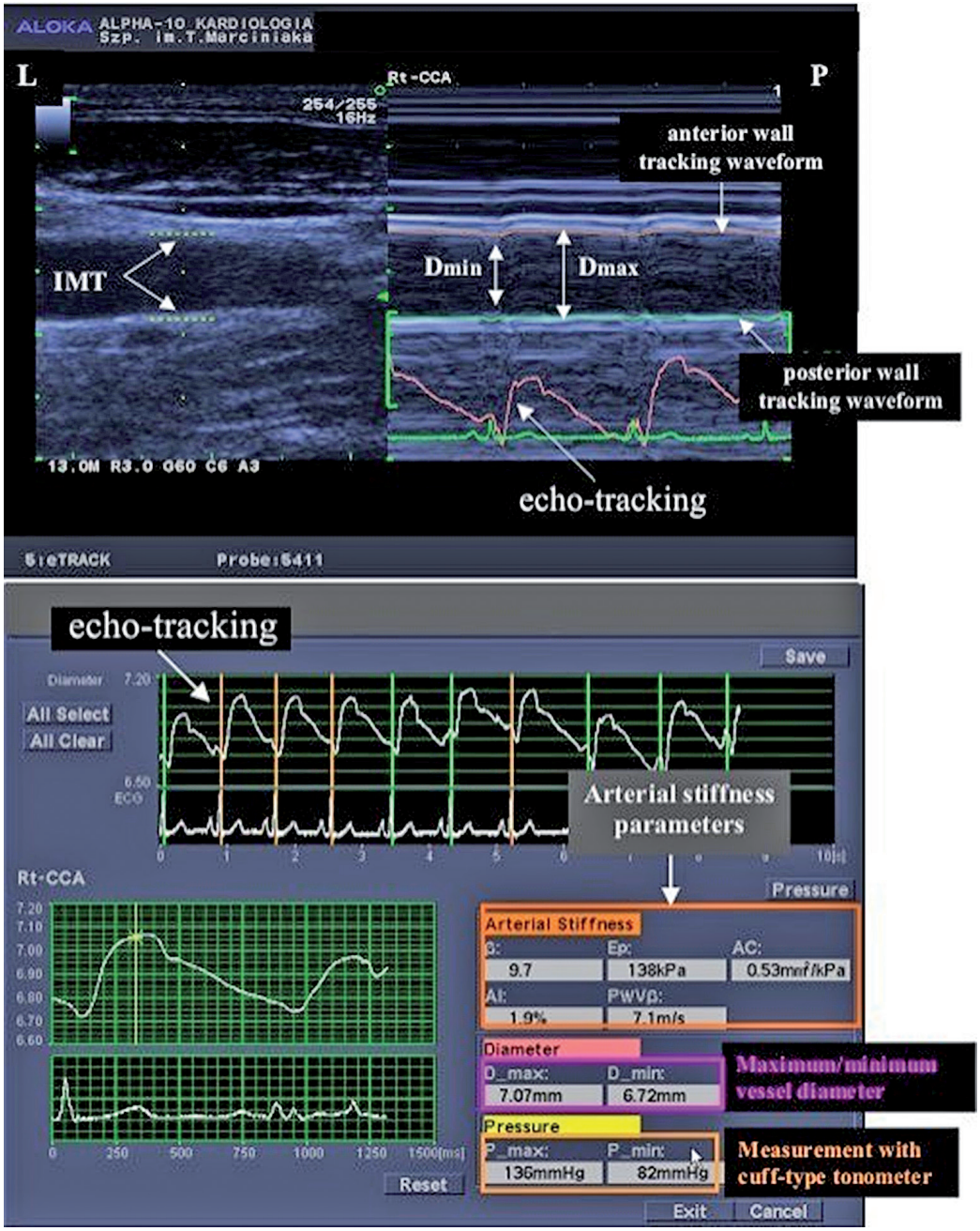

Fig. 2. L/Left – B-mode visualization of right common carotid artery; P/Right – echo-tracking computed curve of dynamic diameter carotid artery. Lower – arterial stiffness parameters: β – beta; Ep – epsilon; AC – arterial compliance; PWVβ – one-point pulse wave velocity; AI – augmentation index

Mean values of β, Ep and PWVβ were significantly higher in the hypertensives with all patterns of LVH and geometry than in the control group (Table 2). Among the hypertensives, mean values of the pressure-strain elasticity modulus were the highest in the CH group (CH vs. N, p = 0.034).

The linear analysis showed significant correlations between the LVH indices and the arterial stiffness parameters (Table 3).

Using the ROC curve analysis, optimal cut-off values were identified for different parameters that can be possible confounding factors in the determination of CH occurrence: age, sex, BMI, cigarette smoking, diabetes, HbA1c, creatinine level, heart rate, systolic and diastolic BP, mean BP, pulse pressure (PP), IMT and arterial stiffness parameters (Table 4).

The univariable analysis revealed the significant variables in determining CH (Table 5). However, in the stepwise forward multivariate analysis only four variables were independently associated with CH occurrence: AI > 21.9% reflecting afterload (OR 3.65, p = 0.003), PWVβ > 7.1 m/s (OR 2.86, p = 0.014), systolic blood pressure (OR 3.12, p = 0037) and the presence of diabetes (OR 3.75, p = 0.007) (Table 5).

Table 1. Clinical characteristics of hypertensive patients with four types of LVH and geometry

	LVH and geometry pattern				P-value
	N (n = 57)	**CR (n = 48)**	**CH (n = 62)**	**EH (n = 35)**	
Age [years]	55.5 ± 12.1	54.0 ± 10.7	58.7 ± 9.0	58.7 ± 7.7	0.051
Man	24 (42%)	25 (52%)	35 (56%)	14 (40%)	0.215
BMI [kg/m^2]	28.7 ± 4.6	29.3 ± 5.2	29.5 ± 4.7	30.3 ± 4.5	0.450
Smoking	20 (35%)	18 (38%)	19 (31%)	9 (26%)	0.977
Diabetes	17 (30%)	20 (42%)	34 (55%)	19 (54%)	0.003
HR [min^{-1}]	70.0 ± 10.1	71.4 ± 9.0	69.7 ± 9.7	66.6 ± 10.7	0.174
BPs [mm Hg]	134.4 ± 14.8	142.2 ± 18.1	144.6 ± 17.9	140.5 ± 17.9	0.013
BPd [mm Hg]	78.6 ± 11.4	84.3 ± 10.8	80.1 ± 11.9	75.9 ± 10.5	0.007
MBP [mm Hg]	97.2 ± 11.5	103.7 ± 11.6	101.6 ± 12.4	97.4 ± 10.6	0.016
PP [mm Hg]	55.7 ± 11.4	57.8 ± 15.4	64.5 ± 14.5	64.5 ± 17.7	0.003
Creatinine [mg/dL]	0.89 ± 0.20	0.89 ± 0.19	0.95 ± 0.22	0.86 ± 0.35	0.798
TCH [mg/dL]	214 ± 42	203 55	198 ± 45	204 ± 47	0.440
HDL [mg/dL]	58 ± 17	54 20	51 ± 13	51 ± 12	0.103
LDL [mg/dL]	127 ± 36	116 44	118 ± 38	122 ± 45	0.616
LVMI [g/m^2]	84 ± 19	88 ± 18	130 ± 33	114 ± 17	p < 0.001

N – normal geometry; CR – concentric remodeling; CH – concentric hypertrophy; EH – eccentric hypertrophy; BMI – body mass index; HR – heart rate; BPs – systolic blood pressure; BPd – diastolic blood pressure; MBP – mean blood pressure; PP – pulse pressure; TCH – triglyceride level; HDL-C –high-density lipoprotein level; LDL-C – low-density lipoprotein level; LVMI – left ventricular mass index.

Table 2. IMT and arterial stiffness indices of control group and hypertensive patients with four types of LVH and geometry

	Control group (n = 60)	LVH and geometry pattern				**P-value**
		N (n = 57)	**CR (n = 48)**	**CH (n = 62)**	**EH (n = 35)**	
IMT [mm]	0.50 ± 0.13	0.63 ± 0.16	0.67 ± 0.22	0.70 ± 0.16	0.68 ± 0.13	p < 0.001*
β [–]	7.0 ± 2.4	8.3 ± 2.9	8.6 ± 2.9	9.7 ± 3.5	9.4 ± 3.7	p < 0.001*
Ep [kPa]	96 ± 39	113 41	123 ± 45	141 ± 56	132 ± 63	p < 0.001*; p = 0.034 (N vs. CH)
AI [%]	17.9 ± 12.7	19.5 ± 19.8	16.5 19.6	20.5 ± 18.1	17.4 ± 10.3	p = 0.727
AC [mm^2/kPa]	0.70 ± 0.24	0.71 ± 0.24	0.70 ± 0.28	0.72 ± 0.32	0.67 ± 0.29	p = 0.936
PWVβ	5.8 ± 1.1	6.2 ± 1.1	6.5 ± 1.1	6.9 ± 1.4	6.6 ± 1.3	p < 0.001*

*p < 0.001 for control group vs. N, CR, CH, EH; IMT – intima-media complex; β – beta stiffness index; Ep – epsilon; AI – augmentation index; AC – arterial compliance; PWVβ – one-point pulse wave velocity; N – normal geometry; CR – concentric remodeling; CH – concentric hypertrophy; EH – eccentric hypertrophy.

Table 3. Linear regression analysis correlations coefficients between LVH indices and arterial stiffness parameters

	β	Ep	AI	AC	PWVβ
LVM	r = 0.084 p = 0.241	r = 0.091 p = 0.206	r = 0.051 p = 0.493	r = 0.012 p = 0.865	r = 0.085 p = 0.238
LVMI	r = 0.167 p = 0.019	r = 0.182 p = 0.011	r = –0.056 p = 0.447	r = 0.093 p = 0.192	r = 0.145 p = 0.042
PWd	r = 0.136 p = 0.058	r = 0.205 p = 0.004	r = –0.137 p = 0.062	r = 0.098 p = 0.173	r = 0.170 p = 0.018
IVSd	r = 0.099 p = 0.169	r = 0.141 p = 0.048	r = –0.026 p = 0.728	r = 0.034 p = 0.634	r = 0.111 p = 0.123
RWT	r = 0.091 p = 0.204	r = 0.173 p = 0.016	r = –0.084 p = 0.253	r = 0.004 p = 0.956	r = 0.148 p = 0.039

LVM – left ventricular mass; LVMI – left ventricular mass index; PWd – posterior wall thickness in diastole; IVSd – interventricular septal thickness in diastole; RWT – relative wall thickness; β – beta stiffness index; Ep – epsilon; AI – augmentation index; AC – arterial compliance; PWVβ – one-point pulse wave velocity.

Table 4. ROC curve analysis in the prediction of the occurrence of concentric hypertrophy

	Cutoff	Sens. (%)	Spec. (%)	PPV (%)	NPV (%)	Accuracy (%)
β (–)	> 8.4	62.7	54.7	37.4	77.3	57.1
Ep (kPa)	> 136	47.5	72.3	42.4	76.2	64.8
AI (%)	> 21.9	44.8	71.9	41.9	74.2	63.2
AC (mm^2/kPa)	≤ 0.58	49.2	58.0	33.3	72.7	55.9
PWV-β (m/s)	> 7.1	45.8	75.9	45.0	76.5	66.8
PWV-WI (m/s)	> 5.5	65.0	53.4	32.5	81.6	56.4
Age (years)	> 50	83.9	29.2	34.9	80.0	46.2
BMI (kg/m^2)	≤ 33	87.1	22.1	33.1	79.5	42.1
HR (min^{-1})	≤ 61	23.7	84.1	38.9	72.0	66.0
BPs (mm Hg)	> 151	37.9	83.3	48.9	76.2	69.9
BPd (mm Hg)	≤ 76	43.1	63.0	32.9	72.5	57.1
MBP (mm Hg)	> 102	48.3	60.1	33.7	73.5	56.6
PP (mm Hg)	> 54	75.9	45.7	37.0	81.8	54.6
Creatinine (mg/dL)	> 0.82	84.6	50.0	33.3	91.7	57.9
IMT (mm)	> 0.56	80.6	37.3	37.3	80.6	51.0
TCH (mg/dL)	≤ 245	93.6	23.8	36.4	88.9	45.9
HDL (mg/dL)	≤ 58	80.9	35.0	36.9	79.5	65.8
LDL (mg/dL)	≤ 169	97.8	13.0	34.1	92.9	39.7
HbA1c (%)	> 7.2	55.6	63.2	44.4	72.9	55.4
Woman	yes	54.8	55.4	24.8	82.1	55.1
Smoking	no	53.7	50.0	31.9	71.2	51.1
Diabetes	yes	77.3	46.2	37.8	82.8	55.4

β – beta stiffness index; Ep – epsilon; AI – augmentation index; AC – arterial compliance; PWVβ – one-point pulse wave velocity; BMI – body mass index; HR – heart rate; BPs – systolic blood pressure; BPd – diastolic blood pressure; MBP – mean blood pressure; PP – pulse pressure; IMT – intima-media complex; TCH – triglyceride level; HDL-C – high-density lipoprotein level; LDL-C – low-density lipoprotein level; HbA1c – glycated hemoglobin.

Table 5. Multiple univariable and multivariable logistic regression analyses to differentiate the occurrence of concentric hypertrophy

	Cutoff	Univariable analysis			Multivariable analysis		
		OR	95% CI	p	OR	95% CI	p
β (–)	> 8.4	2.03	1.09 ÷ 3.80	0.026	–	–	–
Ep (kPa)	> 136	2.35	1.25 4.43	0.008	–	–	–
AI (%)	> 21.9	2.08	1.09 3.96	0.026	3.65	1.53 ÷ 8.62	0.005
AC (mm^2/kPa)	≤ 0.58	0.80	0.42 ÷ 1.51	0.490	–	–	–
PWV-β (m/s)	> 7.1	2.66	1.40 ÷ 5.07	0.003	2.86	1.18 6.66	0.012
Age (years)	> 50	1.74	0.95 3.19	0.074	–	–	–
BMI (kg/m^2)	≤ 33	1.62	0.72 3.66	0.327	–	–	–
HR (min^{-1})	≤ 61	1.24	0.62 ÷ 2.49	0.662	–	–	–
BPs (mm Hg)	> 151	3.06	1.53 6.12	0.002	3.12	1.50 ÷ 6.15	0.037
BPd (mm Hg)	≤ 76	1.05	0.60 1.89	0.999	–	–	–
MBP (mm Hg)	> 102	1.42	0.77 2.63	0.265	–	–	–
PP (mm Hg)	> 54	2.64	1.33 5.26	0.006	–	–	–
Creatinine (mg/dL)	> 0.82	5.50	1.09 ÷ 27.7	0.039	–	–	–
IMT (mm)	> 0.56	2.48	1.21 5.10	0.014	–	–	–
HbA1c (%)	> 7.2	2.15	0.95 4.89	0.103	–	–	–
Woman	yes	1.51	0.86 2.65	0.196	–	–	–
Smoking	no	1.16	0.56 2.41	0.698	–	–	–
Diabetes	yes	2.91	1.30 ÷ 6.51	0.009	3.75	1.43 9.74	0.008

β – beta stiffness index; Ep – epsilon; AI – augmentation index; AC – arterial compliance; PWVβ – one-point pulse wave velocity; HR – heart rate; BPs – systolic blood pressure; BPd – diastolic blood pressure; MBP – mean blood pressure; PP – pulse pressure; IMT – intima-media complex; HbA1c – glycated hemoglobin.

Discussion

The inter-relationship of LVH and arterial damage has been evaluated in both older and more recent papers [2, 5–8] and might have an impact on increased incidence of vascular events, including TIA and stroke, particularly in patients with CH. The CH pattern has consistently been shown to have the worst prognosis [5, 6]. The present study provides evidence on carotid arterial stiffness as a significant confounder of CH occurrence in hypertension.

Carotid Arteries Structural Changes and Left Ventricular Hypertrophy

According to O'Rourke's concept [18], atherosclerosis should be evaluated on the basis of two aspects: atherosis, which reflects structural changes in the intima and media of the vascular wall; and sclerosis, expressing early functional changes in vascular stiffness. The carotid IMT is an index of atherosis, whereas arterial stiffness parameters represent sclerosis [18]. In a previous study, the current authors found that structural changes in the carotid arteries reflected by increased IMT, an indicator of subclinical atherosclerosis, were observed significantly more frequently in patients with CH than in those with other patterns of LV geometry in hypertension [19]. The present study employed integrated ultrasound assessment of IMT, arterial stiffness and wave reflection analysis parameters as well. The univariate analysis in the present study showed that IMT is one of the significant determinants of CH occurrence, among other confounding factors like arterial stiffness and wave reflection parameters, blood pressure components and diabetes (Table 5). However, the influence of IMT disappeared in the multivariate analysis. This suggests that concentric hypertrophy may be more likely to be correlated with carotid function than with carotid wall thickness.

Arterial Stiffness and Left Ventricular Hypertrophy

Arterial stiffening in hypertension results in an increase of LV end-systolic stress, causing LVH. However, arterial stiffness in itself may also play an important role in the development of LVH. Arterial stiffening is responsible for an earlier return of the reflected wave, which would return mainly in systole rather than in diastole, resulting in augmentation of the systolic part of the incident pressure wave, with an increase in central blood pressure and pulse pressure. Thus, increased arterial stiffness might contribute to LVH through an increase in central pulse pressure, independent of mean blood pressure. Data from the Ohasama Study [20] showed that late systolic pressure augmentation is associated with LVH in hypertensive patients. In the present study, the augmentation index was shown to be a significant variable to discriminate patients with CH in the univariate analysis. In the multivariate analysis, AI was associated with CH occurrence independently from MBP and PP (Table 5). This suggests that increased wave reflection contributes to arterial load in CH [21].

Arterial Stiffness and LV Concentric Geometry

Early papers by Boutouyrie et al. [22] and Roman et al. [23] showed a relationship between structural and functional arterial abnormalities and LV remodeling, indicating the occurrence of the ventriculo-arterial coupling phenomenon. Using a high-definition echotracking system, Boutouyrie et al. observed that a reduction in carotid artery distensibility paralleled concentric hypertrophy and remodeling of the left ventricle [22]. Roman et al. provided evidence that arterial stiffness measured by applanation tonometry was related to concentric LV geometry [23].

In a later paper Roman et al. showed that relatively pressure-independent β stiffness and arterial compliance assessed using applanation tonometry were strongly associated with aging and LV concentric remodeling, but the pressure-dependent elastic modulus was associated with LV mass. These results supported the interpretation that β stiffness and the elastic modulus evaluated different aspects of arterial function despite being derived from the same variables [24]. In the present study both pressure-dependent Ep and less dependent β stiffness were observed to correlate significantly with LVMI and RWT. This may be explained by parallel heart and carotid remodeling in hypertension.

To the best of the authors' knowledge, this is the first study to show an independent relationship between local one-point pulse wave velocity (PWVβ) and the CH pattern in middle-aged hypertensives. In the present study, PWVβ was independently associated with CH in the multivariate analysis (OR = 2.18; p = 0.091). The standard index of arterial stiffness is carotid-femoral PWV, because it is simple, reproducible and directly related to the elastic property of arterial walls [9, 10]. However, as noted above carotid-femoral measurements provide the average PWV of various aortic segments that may have quite different elastic properties, whereas the one-point method used in the present study determines PWV locally and provides information about arterial stiffness at a specific region of interest [10]. This may be useful clinically, because the arterial tree is not affected homogeneously by aging and disease. Ultrasound-based carotid stiffness measurements are valuable because they make it possible to determine arterial stiffness in the vessel with the most relevance to particular cerebrovascular outcomes. It was recently shown that local carotid stiffness had independent predictive value for incident stroke, but not for coronary heart disease [25]. In the present study, carotid arterial stiffness was assessed in patients with concentric hypertrophy – the pattern associated with a higher prevalence of carotid atherosclerosis and cerebrovascular events. One-point PWVβ seems to be a novel, promising and easily obtainable parameter, correlated to the "gold standard" carotid-femoral pulse wave velocity [26].

LV Remodeling, Arterial Stiffness and CV Risk Factors

The authors of the Bogalusa Heart Study hypothesized that differences in cardiovascular risk in various types of LV geometry might reflect the differential effects of classic risk factors and arterial stiffness on the left ventricle. They showed that in young adults concentric hypertrophy was associated with widened pulse pressure, the presence of diabetes mellitus, obesity and increased arterial stiffness as assessed by tonometry [27]. In the present study, hypertensives with the CH pattern also had the highest mean values of PP and the elastic modulus of carotid arteries (Ep) measured by the echo-tracking method; diabetes was also more frequent in this group of patients in this study.

In the present study, the presence of diabetes was, as expected, one of the strongest independent determinants of CH. Patients with diabetes tended to have faster PWV and higher AI, both of which were associated with higher LVM than in the controls [28].

The mechanical load on the heart comprises both steady and pulsatile components. Increased

mean arterial pressure, reflecting steady pressure stress, is the key determinant of LVH; increased arterial stiffness as a contributory factor to pulsatile pressure stress also appears to be an important determinant of LVH [29]. Interestingly, the multivariate analysis in the present study showed that both AI and PWVβ were associated with CH, independently of mean blood pressure and along with systolic blood pressure. These results support the hypothesis that arterial stiffness might be a contributory factor to the pulsatile components of blood pressure in the development of CH.

Limitations of the Study

This observational cross-sectional cohort study at two centers is relatively small, and the study group included only Caucasian individuals. Blood pressure values measured over the brachial artery were used to calculate carotid stiffness indices, which might overestimate carotid pressures due to amplification of central to peripheral blood pressure. This phenomenon is important in young subjects, and may have less meaning in the present study due to the mean age of the study population (55.7 ± 10.4 years). Also, echocardiography has certain limitations. The present study included both untreated and treated patients, so that the various types of remodeling would be represented, and interference from active medication with the study results cannot be excluded. Finally, no prognostic follow-up was performed in this study.

Clinical Implications

Arterial stiffness parameters can be easily and quickly obtained from standard carotid ultrasound examinations with little addition to the procedure time, and thus could be implemented by centers performing carotid ultrasound imaging. Echotracking carotid arterial stiffness parameters may serve as simple and easy-to-use early markers of target organ damage, which can be useful in individual and specific management of patients with hypertension. This study may contribute to the creation of a diagnostic and prognostic scoring system for arterial hypertension. This is one of a number of studies indicating that arterial stiffening might be directly involved in the pathophysiology of LVH. Therefore, improving de-stiffening strategies should be one of the major objectives in the prevention and treatment of LVH in hypertension.

Concentric hypertrophy in hypertension is strongly associated with carotid arterial stiffness and wave reflection parameters, independently of the influence of systolic blood pressure and diabetes.

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