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ORIGINAL ARTICLE

The relationship of carotid arterial stiffness to left ventricular diastolic dysfunction in untreated hypertension

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Abstract

Background: Interest in the role of arterial stiffness in the pathomechanism of left ventricular (LV) diastolic dysfunction has grown in recent years.

Aim: To examine the relationship between local carotid arterial stiffness parameters assessed by the ultrasonic high-resolution echo-tracking (eT) method and LV diastolic function indices in patients with untreated hypertension (H).

Methods: The study group consisted of 173 subjects, 78 male and 95 female, 113 of them with untreated H, mean age 55.7 ± ± 10.4 years, and 60 age-matched controls. Using 2D echo, conventional and tissue Doppler echocardiography, LV systolic and diastolic function and left ventricular hypertrophy (LVH) indices were assessed. Hypertensives were divided into two groups: those with diastolic dysfunction (HDD+: with relaxation abnormalities, n = 55 and with pseudonormalisation pattern, n = 12); and those without diastolic dysfunction (HDD–, n = 46). Using carotid arteries ultrasound, intima media thickness (IMT) and eT arterial stiffness parameters were evaluated, as also were β — beta, Ep — epsilon, AC — arterial compliance, PWVβ — one-point pulse wave velocity and AI — augmentation index.

Results: Linear regression analysis revealed significant correlations between arterial stiffness indices and diastolic function parameters in the study groups: the ratio of early to late transmitral pulse Doppler velocities — E/A — correlated to Ep, β, AC and PWVβ ($r = –0.30$, $r = –0.25$, $r = 0.26$, $r = –0.30$, respectively, $p < 0.05$); early diastolic mitral annular velocity — e' — correlated to Ep, β and PWVβ ($r = –0.22$, $r = –0.26$, $r = –0.25$, respectively, $p < 0.05$); the ratio of early to late diastolic mitral annular velocities — e'/a' — was correlated with β and PWVβ ($r = –0.28$, $r = –0.28$, respectively, $p < 0.05$). HDD+ did not present echocardiographic LVH. Using ROC curve analysis, we identified optimal cut-off values of different parameters in the determination of diastolic dysfunction occurrence. Univariable analysis revealed the following significant variables in determining LV diastolic dysfunction: $\beta > 9.2$ (OR 2.65, $p = 0.026$), Ep > 118 kPa (OR 3.53, $p = 0.040$), PWV$\beta > 6.2$ m/s (OR 3.92, $p = 0.002$), AI > 7.8 (OR 2.62, $p = 0.049$), age > 54 (OR 4.76, $p < 0.001$), diabetes presence (OR 2.78, $p = 0.013$), IMT > 0.51 mm (OR 4.49, $p < 0.001$), diastolic blood pressure < 70 mm Hg (OR 3.38, $p = 0.047$), pulse pressure > 64 (OR 2,90, $p = 0.031$) and ejection fraction < 76 (OR 3.38, $p = 0.019$). However, at multivariate analysis, only age (OR = 2.43, $p = 0.073$), IMT (OR = 4.56, $p = 0.002$) and PWVβ (OR = 2.18; $p = 0.091$) were independently associated with diastolic dysfunction occurrence.

Conclusions: Carotid IMT as a marker of subclinical atherosclerosis and PWVβ as an index of carotid arterial stiffness are, besides age, independently associated with LV early diastolic dysfunction occurrence in untreated middle-aged hypertensives.

Key words: arterial stiffness, diastolic dysfunction, hypertension

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INTRODUCTION

Arterial stiffness affects the morbidity and mortality associated with cardiovascular diseases [1, 2]. Although the mechanisms of an increased risk are not fully understood, the promotion of diastolic heart failure has been discussed among them [3, 4]. Left ventricular (LV) diastolic dysfunction, although most frequently diagnosed as the preclinical disease, constitutes a predictor of all-cause mortality [4, 5].

Many factors have been proved to determine LV diastolic function in hypertension [6]. However, the role of arterial stiffness among them has not been fully established yet. Recent studies have investigated the relationship between LV diastolic function and arterial stiffness in different clinical conditions such as diabetes, hypertension and in population-based studies [4, 7, 8], putting the emphasis on arterial-ventricular coupling. It has been proved recently that arterial stiffness increase is responsible for diminished exercise tolerance in subjects with LV diastolic function [9, 10]. These studies have used methods to assess systemic and regional arterial stiffness such as applanation tonometry and mechanotransduction with the evaluation of 'gold standard' carotid-femoral pulse wave velocity [4, 7–13]. However, there is a problem with the clinical use of carotid-femoral pulse wave velocity because of technical difficulties and its low reproducibility. Echo-tracking systems, especially high resolution ones, may provide easy to measure local arterial stiffness parameters in the detection of early functional arterial changes that precede vascular structural remodelling. ESC experts recommend local arterial stiffness measures to pathophysiologic studies [1]. Yet there have been few studies on the relation of local arterial stiffness to LV diastolic function [14–16].

We hypothesised that early functional carotid arterial dysfunction is associated with early LV diastolic function abnormalities in hypertension.

The aim of this study was to examine the relationship between local carotid arterial stiffness parameters assessed by the high resolution echo-tracking method (eT) and LV diastolic function abnormalities from conventional and tissue Doppler echocardiography in patients with untreated hypertension.

METHODS

The study group consisted of 173 subjects, 78 males and 95 females, 113 of them untreated hypertensives, mean age 55.7 ± 10.4 years and 60 age-matched control subjects. Hypertensives were defined as subjects with a history of hypertension (mean duration of disease 2.9 years) in whom the sustained elevation of blood pressure (> 140 mm Hg systolic and/or > 90 mm Hg diastolic) had been observed in at least three separate measurements obtained on different days. All hypertensives were classified as grade I hypertension according to ESC/ESH and were untreated until our study [17]. Patients with diabetes (n = 28) were treated with statins (simvastatine, atorvastatine). Participants were clinically assessed by a cardiologist followed by a screening ECG and echocardiography. Only patients with normal LV systolic function (ejection fraction — EF > 55%) and without cardiomyopathy, pericardial disease or valve dysfunctions were enrolled. Patients with evidence of ischaemic heart disease (a history of angina, history of myocardial infarction, Q waves on ECG and regional wall motion abnormalities on echocardiography) were not eligible for the study.

Vascular ultrasound and high resolution eT of carotid arteries and detailed echocardiography were performed in each subject. The protocol was approved by the local research Ethics Committee and each subject gave his or her informed consent.

High resolution echo-tracking of carotid arteries

Vascular ultrasound of the right common carotid artery was performed with an alpha10 ALOKA machine equipped with an integrated and automated ultrasound, Doppler and eT system. After clear visualisation of intima-media complex of both anterior and posterior arterial wall in its longitudinal axis with maximal internal diameter, an eT sample was positioned at the end of the intima, with 1 kHz sampling rate for continuous detection of carotid diameter changes. In experimental studies, diameter changes are very similar to intravascular pressure changes, something which enables an automatic conversion of carotid diameter waveform changes into arterial pressure waveforms by calibrating its peak and minimal values to systolic and diastolic brachial blood pressures [13]. The relationship of pressure-diameter is thought to be linear [13]. Three to five beats were averaged to obtain a representative waveform. The following arterial stiffness parameters were evaluated on-line [2, 13]:

- β — beta, beta stiffness index, as the ratio of the natural logarithm of systolic/diastolic blood pressure to the relative change in 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, Dd — arterial diastolic diameter,
- Ep — epsilon, Young modulus, pressure-strain elasticity modulus: $Ep = (Ps - Pd)/[(Ds - Dd)/Dd]$,
- AC — arterial compliance, calculated from the arterial cross area and blood pressures: $AC = \pi(Ds \times Ds - Dd \times \times Dd)/[4 \times (Ps - Pd)]$,
- PWVβ — one-point pulse wave velocity, calculated from the time delay between two adjacent distension waveforms from water hammer equation with the usage of β — stiffness parameter: $PWV\beta = \sqrt{(B \times P/2 \times \rho)}$, where P — diastolic blood pressure, ρ — blood density (1,050 kg/m^3).

From the parameters of wave reflection, augmentation index (AI) was calculated as: AI = ΔP/PP, as illustrated in Figure 1.

The blood pressure of the right arm was measured by an automated cuff sphygmomanometer with the patient being in the supine position for 10 min.

There was a good interobserver agreement in arterial stiffness indices values according to the Bland-Altman test; the interobserver intrasession variabilities expressed as coefficient of variation (%) were as follows: β — 5.4%, Ep — 4.6%, PWVβ — 3.9%, AC — 3.9%, AI — 4.3%.

Original example of arterial stiffness parameters examination by high resolution eT system derived from right common carotid artery is presented in Figure 2.

Intima media thickness (IMT) was determined according to the established standards [18].

Echocardiography

A detailed two-dimensional Doppler echocardiogram (alpha 10 ALOKA, Japan) was recorded for all the patients. M-mode measurements of end diastolic wall thickness (of interventricular septum — IVS and posterior wall — PW) and cavity diameter (LV end-diastolic diameter — EDD) were used to calculate LV mass (LVM) by the formula introduced by Devereux et al. [19] and indexed to body surface area (BSA) to obtain LV mass index (LVMI). Relative wall thickness (RWT) was calculated using the formula: RWT = 2PW/EDD.

Left ventricular hypertrophy (LVH) was diagnosed when LVMI > 110 g/m^2 in women and > 125 g/m^2 in men [17].

LV systolic function was assessed by endocardial fractional shortening (FS), ejection fraction (EF) was estimated using the Teichholtz method, and mid-wall fractional shortening (mFS) was obtained using the de Simone method [20]. Assessment of LV diastolic function included transmitral pulse wave Doppler with evaluation of early (E) and late (A) velocities, E/A ratio, E wave deceleration time (DTE) as well as tissue Doppler imaging parameters with early (e') and late (a') diastolic mitral annular velocities measured and averaged from septal and lateral sides of mitral annulus with their ratio — e'/a'. E/e' ratio as an index of LV filling pressure was calculated. Isovolumic relaxation time (IVRT) was measured from the end of aortic flow to the beginning of mitral inflow with the simultaneous visualisation of aortic and mitral flow. Doppler parameters were averaged from three measurements.

Diastolic dysfunction was diagnosed according to the recent recommendations [21] with the following diagnostic criteria for:

- grade I — mild diastolic dysfunction — impaired relaxation: mitral E/A ratio < 0.8; DTE > 200 ms; e' < 8 cm/s; E/e' < 8 g
- grade II — moderate diastolic dysfunction — impaired relaxation with mild to moderate elevation of LV filling pressure: mitral E/A ratio 0.8–1.5 (pseudonormal) with decrease by > 50% during the Valsalva manoeuvre; DTE 160–200 ms; e' < 8 cm/s; E/e' 9–12;
- grade III — severe diastolic dysfunction — restrictive LV filling: E/A ≥ 2; DTE < 160 ms; E/e' > 13.

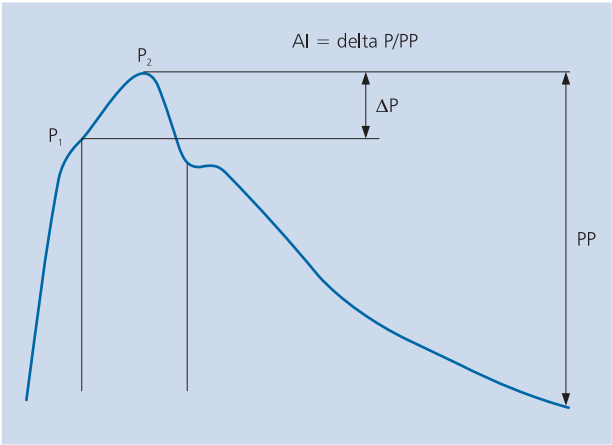

Figure 1. Augmentation index (AI) — method of calculation [1]; PP — pulse pressure, P_1 — first systolic peak, P_2 — second systolic peak, delta P = $P_2 - P_1$

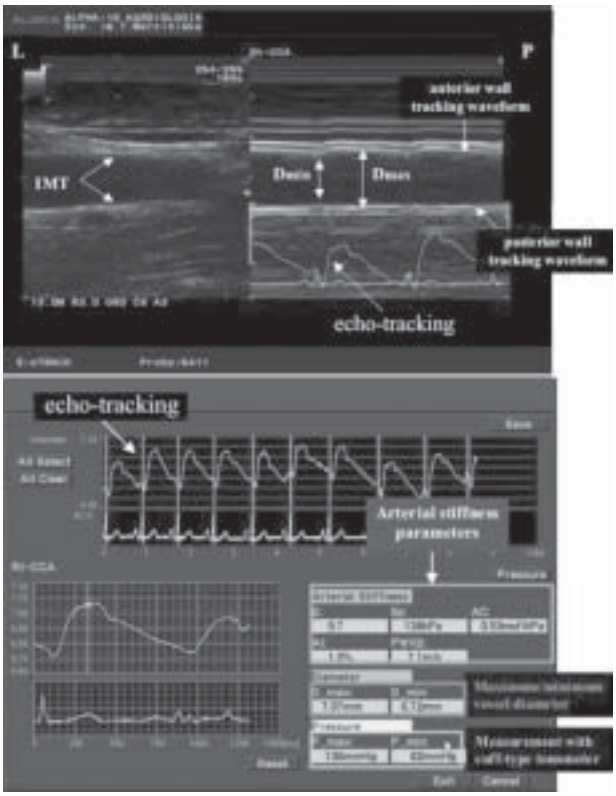

Figure 2. L-Left: B-mode visualisation of right common carotid artery. **P-Right:** Echo-tracking computed curve of dynamic diameter carotid artery. **Lower:** Arterial stiffness parameters: β — beta; Ep — epsilon; AC — arterial compliance; PWVβ — one-point pulse wave velocity; AI — augmentation index

Hypertensives were divided into two groups: with diastolic dysfunction (HDD+, n = 67), and without diastolic dysfunction (HDD–, n = 46). Grade I — mild diastolic dysfunction in a model of relaxation abnormalities was noted in 55 hypertensives; grade II — moderate diastolic dysfunction (pseudonormalisation pattern) was observed in 12 patients. None of the study subjects, untreated hypertensives with a short duration of the disease, presented severe diastolic dysfunction with restrictive LV filling.

Statistical analysis

Mean and standard deviations were calculated for quantitative variables and percentages for qualitative variables. All variables were not-normally distributed, and therefore differences between groups were tested by Mann-Whitney test for quantitative variables and by χ^2 test for percentages of qualitative variables. The statistical significance was set at $p < 0.05$ (two-sided tests), and for multiple testing we used a statistical significance of $p < 0.01$). Interobserver variability was assessed by comparing the readings of the two observers; Bland-Altman analysis was used. For quantitative variables that showed a statistically significant difference between the two groups, receiver-operating characteristic (ROC) curves were obtained to calculate the cut-off values optimised to reach the best compromise in the prediction of diastolic dysfunction. Optimal cut-off was defined as a threshold where the sum of sensitivity and specificity was maximum.

A multivariable logistic regression analysis was conducted considering as dependent variables the occurrence of diastolic dysfunction. All the variables presenting a significant value < 0.25 at univariate analysis were included in the model. The stepwise method with backward elimination was used, and odds ratios (OR) with 95% CIs were calculated. The model was evaluated using the Hosmer-Lemeshow test.

RESULTS

The study group's characteristics are presented in Table 1. Hypertensives with diastolic dysfunction (HDD+) were, on average, 7.1 years older than those without diastolic dysfunction (HDD–). There were no significant differences in the prevalence of gender, smoking, hypercholesterolaemia, obesity, heart rate, clinical systolic and diastolic blood pressures and LVH occurrence between the two groups. The mean values of LVMI in HDD+ did not meet the criteria for LVH. HDD+ were more likely to have diabetes. LV systolic function was preserved in all study subjects. All patients had normal IMT values, although the mean values of IMT were significantly higher in HDD + than in HDD–.

The arithmetic mean values of carotid high resolution eT arterial stiffness and wave reflection indices were established in control group (with 95% CI for the mean, with the use of the D'Agostino-Pearson test for normal distribution (Table 2). The mean values of carotid arterial stiffness indices: β, Ep and PWVβ were significantly higher in HDD+ than in HDD– (Table 3). The influence of age on carotid arterial stiffness indices was corrected with the use of linear regression equations derived from control group assessments. Regression coefficients (slope) in the control group were as following:

β: +0.071 [1/year];
Ep: +1.52 [kPa/year];
AC: –0.06 [mm^2/(kPa/year)];
PWV: +0.04 [m/(s/year)];
AI: +0.38 [%/year].

Linear regression analysis revealed significant correlations between arterial stiffness indices and diastolic dysfunction parameters in the study groups (Table 4): E/A correlated to Ep, β, AC and PWVβ ($p < 0.05$); e' correlated to Ep, β and PWVβ ($p < 0.05$); e'/a' was correlated with β and PWVβ ($p < 0.05$).

Using ROC curve analysis, optimal cut-off values of different parameters in the determination of diastolic dysfunction occurrence were identified.

Univariable analysis revealed the following significant variables in determining LV diastolic dysfunction (Table 5): $\beta > 9.2$, Ep > 118 kPa, PWV$\beta > 6.2$ m/s, AI > 7.8, age > 54, diabetes presence, IMT > 0.51 mm, diastolic blood pressure < 70 mm Hg, pulse pressure > 64 and EF < 76.

However, at multivariate analysis, only age, IMT and PWVβ were independently associated with LV diastolic dysfunction occurrence (Table 5).

DISCUSSION

Left ventricular diastolic dysfunction is one of the earliest cardiac changes in hypertensive heart disease. It may occur in hypertensives with normal LV systolic function and precipitate heart failure in these patients. LV diastolic function abnormalities may precede left ventricular hypertrophy [21]. In our study, hypertensives with diastolic dysfunction did not present echocardiographic LVH.

Previous studies have demonstrated that LV diastolic dysfunction in hypertension is influenced by age, heart rate, blood pressure components, load conditions, LVH, LV systolic performance and sympatho-vagal balance [6]. Recently, reduced aortic distensibility has been reported in patients with diastolic heart failure and correlated with exercise limitation in these patients [8]. Heart failure with preserved EF is not solely a diastolic disease but is also characterised by systolic-ventricular and arterial stiffening with adverse coupling between the systems [9, 10]. Patients with increased arterial stiffness have lower systolic reserve in response to exercise. Several studies have reported coupling of ventricular-vascular function while investigating the relationship between systemic or regional arterial stiffness (from applanation tonometry, quite poorly available in daily clinical routine) and LV diastolic function in different clinical conditions [4, 7–11].

Still little is known about the relation of local arterial stiffness to LV diastolic function in hypertension. Echo-tracking

Table 1. Clinical and echocardiographic characteristics of the study groups

	HDD+ (n = 67)	HDD– (n = 46)	P: HDD– *vs* HDD+
Age [years]	58.8 ± 9.3	50.9 ± 10.3	**0.0002**
BMI [kg/m^2]	29.13 ± 4.16	28.63 ± 4.79	0.656
Sex	55%M/45%F	51%M/49%F	0.558
Diabetes	35%	13%	**0.011**
Smokers	13%	10%	0.762
Cholesterol [mg/dL]	210 ± 21	229 ± 23	0.117
LDL-C [mg/dL]	128 ± 19	136 ± 20	0.411
HDL-C [mg/dL]	48 ± 6.5	55 ± 7.5	0.168
TGL [mg/dL]	171 ± 16	180 ± 18	0.218
IMT [mm]	0.68 ± 0.22	0.56 ± 0.13	**0.0018**
HR [1/min]	70.5 ± 9.5	71.8 ± 10.1	0.483
Ps [mm Hg]	143 ± 19	141 ± 20	0.554
Pd [mm Hg]	78 ± 11	81 ± 11	0.119
EF [%]	72.3 ± 7.6	68.8 ± 7.1	0.154
mFS%	16.6 ± 2.5	16.6 ± 2.8	0.865
RWT [–]	0.418 ± 0.095	0.452 ± 0.089	0.448
IVSd [mm]	10.9 ± 2.1	12.2 ± 2.0	0.098
PWd [mm]	9.8 ± 2.4	10.9 ± 2.0	0.236
LVMI [g/m^2]	94.4 ± 21.3	113.9 ± 31.3	0.164
e' [cm/s]	7.3 ± 1.6	9.9 ± 1.8	**< 0.001**
E/A [–]	1.00 ± 0.37	1.34 ± 0.31	**< 0.001**
e'/a' [–]	0.72 ± 0.14	1.17 ± 0.22	**< 0.001**
IVRT [ms]	105.7 ± 27.8	90.6 ± 26.6	**0.001**
DTE [ms]	192.9 ± 48.1	171.7 ± 48.5	**0.006**
E/e' [–]	10.04 ± 3.28	8.33 ± 2.03	0.292

p ≤ 0.01 considered significant; HDD+ — hypertensives with diastolic dysfunction; HDD– — hypertensives without diastolic dysfunction; BMI — body mass index; M — males; F — females; LDL-C — low density lipoproteins level cholesterol; HDL-C — high density lipoproteins level cholesterol; TGL — triglycerides level; IMT — intima-media complex; HR — heart rate; Ps — systolic blood pressure; Pd — diastolic blood pressure; PP — pulse pressure; EF — ejection fraction; mFS% — mid-wall fractional shortening; RWT — relative wall thickness; IVSd — inter-ventricular septal thickness in diastole; PWd — posterior wall thickness in diastole; LVMI — left ventricular mass index; e' — early mitral diastolic annular velocity; a' — atrial mitral diastolic annular velocity; E — early mitral inflow velocity wave; A — late mitral inflow velocity wave; IVRT — isovolumic relaxation time; DTE — E wave deceleration time

Table 2. Arithmetic mean values of echo-tracking arterial stiffness indices in a healthy population (95% CI for the mean, D'Agostino-Pearson test for normal distribution)

	Mean	95% CI	P
β [–]	7.35	6.63–8.07	0.664
Ep [kPa]	95.3	81.5–109.1	0.061
AC [mm^2/kPa]	0.75	0.69–0.81	0.096
AI [%]	14.1	10.8–17.4	0.062
PWVβ [m/s]	5.85	5.49–6.21	0.614

β — beta stiffness index; Ep — epsilon; AC — arterial compliance; AI — augmentation index; PWVβ — one-point pulse wave velocity

systems, recommended by ESC experts to mechanistic analyses in pathophysiologic studies, may be useful in the early detection of functional arterial changes [1, 15, 22]. A major advantage is that local arterial stiffness is directly determined from the change in pressure driving the change in volume without using assumptions from a model of the circulation [1].

To the best of our knowledge, this is the first study to determine the relationship between eT local carotid arterial stiffness and early LV diastolic dysfunction in untreated middle-aged hypertensives. In our material, we noted early diastolic function disturbances in the forms of slowed relaxation and pseudonormalisation patterns; it is interesting that subjects with diastolic dysfunction did not show echocardiographic LVH.

In our study, as we expected, univariable analysis revealed age, diabetes, blood pressure components and EF to be significant variables in determining LV diastolic dysfunction in hypertensives.

Table 3. Echo-tracking arterial stiffness indices in hypertensives with and without diastolic dysfunction

	Healthy subjects	HDD+	HDD–	P
β [–]	8.3 ± 2.2	10.8 ± 3.6	9.3 ± 2.8	**0.028***
Ep [kPa]	116.8 ± 44.1	155.5 ± 57.9	126.2 ± 45.8	**0.01***
AC [mm²/kPa]	0.66 ± 0.19	0.67 ± 0.29	0.71 ± 0.28	0.451
AI [%]	14.1 ± 11.7	19.5 ± 12.4	16.8 ±11.1	0.060
PWVβ [m/s]	6.4 ± 1.1	7.2 ± 1.3	6.6 ± 1.2	**0.02***

*p < 0.05 considered significant; abbreviations as in Tables 1 and 2

Table 4. Linear regression correlation coefficients between left ventricular diastolic function indices and arterial stiffness indices in the study group

Diastolic function indices	Arterial stiffness indices				
	Ep	β	AC	AI	PWVβ
e'	**–0.22***	**–0.26***	0.13	–0.07	**–0.25***
E/A	**–0.30***	**–0.25***	**0.26***	–0.06	**–0.30***
e'/a'	0.01	**–0.28***	0.16	–0.12	**–0.28***
IVRT	0.13	0.15	–0.08	0.09	0.15
DTE	0.08	0.05	0.07	–0.12	0.08

*Correlation coefficients at p < 0.05 considered significant; abbreviations as in Tables 1 and 2

Table 5. Multiple logistic regression analysis for the discrimination of left ventricular diastolic dysfunction

Variables	Cut-off value	Univariable analysis			Multivariable analysis		
		OR	95% CI	P	OR	95% CI	P
β [–]	> 9.2	2.65	1.12–6.27	**0.026**			
Ep [kPa]	> 118	3.53	1.49–8.33	**0.040**			
AC [mm²/kPa]	≤ 0.58	1.96	0.83–4.63	0.126			
AI [%]	> 7.8	2.62	1.02–7.32	**0.049**			
PWVβ [m/s]	> 6.2	3.92	1.65–9.33	**0.002**	**2.18**	**1.03–5.78**	**0.091**
Age [years]	> 54	4.76	2.08–10.9	**< 0.001**	**2.43**	**1.12–6.79**	**0.073**
Sex	Male	1.25	0.59–2.68	0.569			
BMI [kg/m²]	28.1	1.69	0.76–3.76	0.228			
Diabetes	Yes	2.78	1.25–6.19	**0.013**			
Hypercholesterolaemia	Yes	2.24	1.04–4.82	0.055			
Smokers	No	1.15	0.46–2.91	0.814			
IMT [mm]	> 0.51	4.49	1.89–10.7	**< 0.001**	**4.56**	**1.73–12.1**	**0.002**
HR [1/min]	≤ 68	1.96	0.84–4.56	0.146			
Ps [mm Hg]	> 151	1.96	0.70–5.49	0.231			
Pd [mm Hg]	≤ 70	3.38	1.05–10.9	**0.047**			
PP [mm Hg]	> 64	2.90	1.15–7.33	**0.031**			
EF [%]	≤ 76	3.86	1.19–12.6	**0.019**			
mFS%	≤ 15.5	1.77	0.65–4.80	0.337			
LVMI [g/m²]	> 134	2.55	0.41–15.7	0.059			
Hosmer-Lemeshow test						$\chi^2 = 23.07$	< 0.0001

HDD = –1.23 + 1.52 × IMT + 0.89 × Age + 1.98 × PWVβ, $R^2 = 0.796$

Abbreviations as in Tables 1 and 2

It is clear that ageing accelerates both diastolic dysfunction and arterial stiffness development. In a multi-centre study (nine European centres including our site) the impact of age on carotid arterial stiffness on a healthy population was noted [23]. The influence of age on arterial stiffness and wave reflection indices was corrected with the use of linear regression equations derived from control group assessments with regression coefficients reported in the results. After adjustments, age still appeared to be one of the most independent determinants of diastolic dysfunction occurrence in a multivariate analysis (Table 5).

Abhayaratna et al. [4, 11] showed that age-related deterioration in diastolic dysfunction was independently associated with increasing aortic stiffness measured by pulse wave velocity from applanation tonometry. In our study, one-point pulse wave velocity (PWVβ) was independently associated with diastolic dysfunction occurrence in multivariate analysis (OR = 2.18; p = 0.091).

This new eT local stiffness parameter — PWVβ — one-point pulse wave velocity, differently defined from the 'gold standard' carotid-femoral pulse wave velocity designed to assess regional arterial stiffness, seems to be a novel and easy to measure parameter, yet still correlated to the 'gold standard' one [24].

In our study, linear analysis revealed significant correlations between arterial stiffness indices and diastolic dysfunction parameters from conventional and TDI Doppler echocardiography in all study groups (Table 4). The group of Avgeropoulou et al. [16] showed a significant inverse relationship between mitral early myocardial diastolic velocity and eT arterial stiffness parameters such as Ep, β and PWVβ in diabetes patients. Also Fraser's group observed in normal subjects and in different pathologic conditions that eT stiffness parameter β was inversely and independently related to longitudinal early diastolic mitral annular velocity, and suggested that non-invasive assessment of the β index might be useful for studying the effects on arterial stiffness of treatment designed to optimise ventriculo-arterial coupling and cardiac performance [15].

Mottram et al. [3] showed that arterial compliance from applanation tonometry was independently associated with diastolic dysfunction in hypertension, and they suggested a possible mechanistic link between arterial compliance and diastolic heart failure. Increased arterial stiffness is associated with a higher velocity of transmission of the pulse wave generated by LV ejection. Early return of reflected waves that arrive back during LV systole may lead to augmentation of the central aortic pressure wave amplitude, thus increasing LV afterload and central aortic pressure [3, 25]. Increased afterload may promote LVH and may also directly slow LV relaxation. Relaxation abnormalities were the main pattern of LV diastolic dysfunction in our hypertensives. The concomitant reduction in central diastolic blood pressure may compromise coronary perfusion, which, in an association with LVH and increased afterload, may exacerbate subendocardial ischaemia. This can further impair LV relaxation and promote interstitial fibrosis leading to reduced LV compliance. Interaction of these processes may be important in the clinical expression of heart failure [8]. Of the eT wave reflection parameters in our study, AI tended to be higher in hypertensives with LV diastolic dysfunction, although it was not statistically significant. Augmentation index was one of the significant variables to discriminate patients with LV diastolic dysfunction in univariate analysis. However, it is known from other studies that augmentation index demonstrates a 'plateau phenomenon' after a certain age in both men and women, something which results from diminished impedance mismatch between central and peripheral arteries affected by change in wave reflection site with ageing [26].

In our study, multivariate analysis revealed that also IMT was independently associated with the occurrence of diastolic dysfunction (OR = 4.56, p = 0.0004), although all patients had normal and low IMT values. In the study by Mizuguchi et al. [14], the LV relaxation from strain imaging was shown to be significantly associated with carotid arterial atherosclerosis in patients with cardiovascular risk factors. Atherosclerosis should be evaluated based on two aspects: atherosis, which reflects structural changes in the intima and media of the vascular wall, and sclerosis, which reflects early changes in vascular stiffness. The carotid IMT is an index of atherosis, whereas arterial stiffness parameters represent sclerosis [14]. In our study, increased arterial stiffness parameters in patients with LV diastolic dysfunction were observed, which supports the need for early detection of vascular pathophysiologic changes in preventing the development to vascular diseases and for treating these disorders in the early stages before a severe outcome occurs. Exercise and effective medication such as converting enzyme inhibitors, angiotensin receptor antagonists and statins may improve vascular elasticity, and furthermore directly improve LV diastolic function.

Therefore, the results of our study may be important in considering diagnostic and therapeutic strategies aimed at cardiac protection [1].

Limitations of the study

The study population was relatively small, only Caucasian and well-educated, which limits the capacity of our findings to be generalised. Blood pressure values used to calculate carotid eT arterial stiffness indices were measured over the brachial artery, which tends to overestimate carotid pressures due to central to peripheral blood pressure amplification. This is especially important in young subjects, but may have less relevance due to the mean age of our study patients which was 55.7 ± ± 10.4 years. The material consisted only of early grades of diastolic dysfunction, thus the relationship between arterial stiffness and advanced forms of diastolic dysfunction was not

analysed. The influence of hypoglycaemic and hypolypaemic therapy in 28 subjects on arterial stiffness is hardly to be excluded.

Future studies should investigate arterio-ventricular coupling, and whether strategies to reduce vascular stiffness can diminish LV diastolic dysfunction and the prevalence of failure.

CONCLUSIONS

Carotid IMT as a marker of subclinical atherosclerosis, and PWVβ as an index of carotid arterial stiffness are, besides age, independently associated with LV early diastolic dysfunction occurrence in untreated middle-aged hypertensives.

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Zależności między sztywnością tętnic szyjnych a zaburzeniami czynności rozkurczowej lewej komory w nadciśnieniu tętniczym

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Streszczenie

Wstęp: W ostatnim czasie wzrasta zainteresowanie udziałem sztywności tętnic w patomechanizmie dysfunkcji rozkurczowej lewej komory (LV) w nadciśnieniu tętniczym.

Cel: Celem pracy było zbadanie zależności między parametrami sztywności tętnic szyjnych ocenianymi ultrasonograficzną metodą *echotracking* o wysokiej rozdzielczości (eT) a wskaźnikami funkcji rozkurczowej LV u pacjentów z nieleczonym dotychczas nadciśnieniem tętniczym.

Metody: Badania przeprowadzono u 173 osób, 78 mężczyzn i 95 kobiet, w tym u 113 z nieleczonym dotychczas nadciśnieniem tętniczym, ze średnią wieku 55,7 ± 10,4 roku i u 60 osób z grupy kontrolnej. Echokardiograficznie, w tym przy zastosowaniu konwencjonalnych i tkankowych metod doplerowskich, oceniono wskaźniki funkcji skurczowej i rozkurczowej LV. Chorych na nadciśnienie podzielono na 2 grupy: bez dysfunkcji rozkurczowej LV (HDD–, n = 46) oraz z dysfunkcją rozkurczową LV (HDD+), w tym: z zaburzeniami relaksacji (n = 55) i z modelem pseudonormalizacji (n = 12). W badaniu USG tętnic szyjnych oceniono grubość kompleksu błony wewnętrznej i środkowej (IMT), a w badaniu eT — parametry sztywności tętnic szyjnych: β — beta, Ep — epsilon, AC — podatność naczyń, PWVβ — jednopunktową prędkość fali tętna, a także AI — wskaźnik wzmocnienia.

Wyniki: Analiza regresji liniowej wykazała istotne korelacje między wskaźnikami sztywności tętnic a parametrami dysfunkcji rozkurczowej LV: wskaźnik prędkości maksymalnej wczesnej fali napływu mitralnego do prędkości maksymalnej fali napływu mitralnego po skurczu przedsionka (E/A) korelował z Ep, β, AC i PWVβ (r = –0,30; r = –0,25; r = 0,26; r = –0,30, odpowiednio $p < 0,05$); maksymalna prędkość wczesnorozkurczowego ruchu pierścienia zastawki mitralnej (e') korelowała z Ep, β i PWVβ (r = –0,22; r = –0,26; r = –0,25, odpowiednio $p < 0,05$); stosunek e' do maksymalnej prędkości ruchu pierścienia zastawki mitralnej po skurczu przedsionka (e'/a') korelował z β i PWVβ (r = –0,28; r = –0,28, odpowiednio $p < 0,05$). Metodą analizy krzywej ROC ustalono optymalne wartości odcięcia dla poszczególnych czynników determinujących występowanie dysfunkcji rozkurczowej LV. Na podstawie analizy jednoczynnikowej zidentyfikowano następujące istotne czynniki związane z występowaniem dysfunkcji rozkurczowej LV: $\beta > 9,2$ (OR 2,65; p = 0,026), Ep > 118 kPa (OR 3,53; p = 0,040), PWV$\beta > 6,2$ m/s (OR 3,92; p = 0,002), AI > 7,8 (OR 2,62; p = 0,049), wiek > 54 lata (OR 4,76; $p < 0,001$), obecność cukrzycy (OR 2,78; p = 0,013), IMT > 0,51 mm (OR 4,49; $p < 0,001$), ciśnienie rozkurczowe < 70 mm Hg (OR 3,38; p = 0,047), ciśnienie tętna > 64 (OR 2,90; p = 0,031) i frakcję wyrzutową < 76 (OR 3,38; p = 0,019). Jakkolwiek, w analizie wieloczynnikowej tylko wiek (OR = 2,43; p = 0,073), IMT (OR = 4,56; p = 0,002) i PWVβ (OR = 2,18; p = 0,091) były niezależnie związane z występowaniem dysfunkcji rozkurczowej LV.

Wnioski: Wiek, IMT tętnic szyjnych jako marker subklinicznej miażdżycy oraz PWVβ jako wskaźnik sztywności tętnic szyjnych są niezależnie związane z występowaniem dysfunkcji rozkurczowej lewej komory u pacjentów z nieleczonym dotychczas nadciśnieniem tętniczym.

Słowa kluczowe: sztywność tętnic, dysfunkcja rozkurczowa lewej komory, nadciśnienie tętnicze

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