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Systolic and diastolic function in hypertension

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Abstract

The consequences of hypertension on the heart in addition to hypertrophy of the left ventricle (LV) are systolic and diastolic dysfunction as a result of disturbances in contractility, relaxation and filling of LV. The study included 449 patients with a hypertension (HTA). Patients with hypertension were examined by echocardiography (M-mode, two-dimensional, pulse and tissue Doppler). We found that only 7.1% of patients with HTA had ejection fraction (EF) < 45%, while the diastolic dysfunction (DD) - the ratio early (E) to late (A) filling velocity (E/A<0.74) was discovered in 32.5%. EF has significantly influenced the symptoms predominantly dyspnea (p<0.02). Many patients had E to annular early fillinig velocity (Ea) E/Ea ratio > 8 (74.6%). LA size was significant for DD and E/Ea ratio (p = 0.017, p=0.018 respectively). The E/A ratio was significantly influenced by duration of HTA (p=0.017). A small number of patients with HTA had an ejection fraction < 45%, but the dyspnea was significantly more common in these patients. Diastolic dysfunction and E/Ea ratio > 8 were frequent in patients with hypertension and were significant influenced by LA size. The E/A ratio was affected by duration of HTA.

Keywords: echocardiography, hypertension, tissue Doppler, E/Ea ratio, left atrium size, ejection fraction

Introduction

It is estimated that the hypertension (HTA), leading risk factor, that has caused 7.5 million deaths in 2008 [1]. HTA is responsible for at least 45% of deaths due to hypertensive heart disease [1].

It is recognized that the left ventricular hypertrophy (LVH), a common finding in hypertensive patients [2].

According investigation of Institute of Statistics of Montenegro in 2008, in Montenegro the average systolic blood pressure (BP) in the adult population (20 years and over), was 131.3 mmHg and 32.7% have hypertension - elevated systolic (≥140mmHg) or diastolic (≥90mmHg) blood pressure, or who had been taking medications to reduce blood pressure.

LVH diagnosis is established if exists wall thickness or dilatation of the LV cavity or both [2]. Compensatory mechanism for hemodynamic load is the increase in mass due to the hypertrophy of existing myocytes rather than hyperplasia as a result of increase in myocyte width for parallel extensions sarcomeres which results in an increase in wall thickness [3]. There are records that angiotensin II (Ang II) is the main growth factor of the heart, in addition to hypertrophy of cardiac myocytes and also causes mitogenesis of cardiac fibroblasts in vitro mimic those of growth factor in vitro and

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response of the load-induced hypertrophy in vivo [4]. In the LVH that accompanies hypertension, the extracellular space is the site of an abnormal fibrillar collagen accumulation [5-6]. This progressive interstitial and perivascular fibrosis accounts for abnormal myocardial stiffness and ultimately ventricular dysfunction and is likely a result of cardiac fibroblast growth and enhanced collagen synthesis [6].

Studies have shown that isolated diastolic dysfunction often accompanies hypertensive disease [7]. Pressure overload leads myocardial fibrosis, LVH, and impaired diastolic filling without systolic dysfunction [8]. Terms active ventricular relaxation and passive filling have appeared since 1970. [9]. Many studies showed the impact of myocardial fibrosis in the diastolic dysfunction [10]. Reduction of diastolic LV extensibility is also found in disorders of energy balance of the myocardium and ischemia [11]. Delayed relaxation can affected many factors that disturb the structure-function relaxation of myofilaments- from alterations at the molecular level to the exposure of the heart to high filling volume (preload), and increased wall stress and arterial impedance (afterload) [10]. Fatigue, dyspnea, reduced exercise tolerance, and peripheral edema are common presenting complaints in hypertensive patients with diastolic dysfunction [8]. Many authors emphasize that the symptoms of cardiac failure, exertional dyspnea including, fluid retention, have yet apparent preservation of systolic function [10] . To measure the systolic function used measurement of dimensions and volumes in systole and diastole to calculate the ejection fraction (EF), and the introduction of Doppler technique enables measurement of blood flow within the heart and diastolic function of the heart.

Long axis connecting the apex of the heart, which is considered to be fixed relative to the base of the heart, which is located at the atrioventricular ring [12]. It is possible to determine the changes in the long axis of the heart by measuring the motion of the mitral ring [12]. Thus, the tissue Doppler appeared alternative method for testing the global and regional contractility [13].

Measurements can be made by pulsed Doppler and the pulse wave is used to determine the maximum speed of myocardium particularly along the longitudinal axis as the longitudinal fibers parallel to the Doppler signal and the movement of the mitral annulus and is a good surrogate for measuring the total longitudinal myocardial contraction and relaxation [14]. Visualization is obtained movement in systole and reverse two-phase- movement long axis toward apex in systole and reverse biphasic movement during isovolumic period [15]. According the results of many studies of all echocardiographic parameters it was found that LV filling index E/Ea (lateral) derived from Doppler of mitral flow E wave and Ea of tissue Doppler was identified as the best index to detect diastolic dysfunction in heart failure with normal EF (HFNEF) in which the diagnosis of diastolic dysfunction was confirmed by conductance catheter analysis [16]. However, an elevated E/Ea which indicates the presence of diastolic dysfunction (in a symptomatic patient), was not evaluated as

Table 1. Basal characteristics.

Characteristics	Number	Percent
Age	59.21±10.087	
Male %	143	31.9
Waist	98.49±14.116	
Mean Systolic BP	149.27±21.874	
Mean Diastolic BP	92.35±11.629	
BMI	30.1	
Smoking	120	26.7
Pos. family his.for CD	185	41.2
Pos. family his.for HTA	229	51.0
Glucose	6.23±1.810	
Cholesterol	5.631±1.188	
HDL	1.422± .770	
LDL	3.873±6.101	
Trigliceride	1.923±1.478	
BNP	21.801±39.328	
Beta-blockers	233	51.9
ACE-inhibitors	282	62.8
Diuretics	23	5.1
Ca antagonists	159	35.4
ARBs	23	5.1
ACE-inhibitors+diuretics	254	58.0
1 drug	109	24.3
2 drugs	142	31.6
3 drugs	117	26.1
> 3 drugs	69	15.7
Mean duration of HTA	12.82±21.331 yrs	

BP-blood pressure, BMI - body mass index, CD - coronary disease, HDL - high density lipoproteins, LDL - low density lipoproteins, BNP - brain natriuretic peptide, Ca antagonist-calcium anagonists, ARBs - AT2 receptors blockers, ACE - angiotensin converting enzyme.

Table 2. Echocardiographic characteristics.

Characteristics	Mean	Std. Deviation
EDD	48.235	28.707
ESD	31.658	11.459
Septum thickness	9.97	5.305
Posterior wall thickness	10.08	7.662
EF	58.63	9.41
LA	38.70	17.07
E wave	.8412	1.88285
A wave	.8292	.22997
E/A	.8727	.32592
Sa	.1724	.23421
Ea	.2177	.29212
Aa	.2622	.35822
E/Ea	7.634	27.3931

EDD-end diastolic dimension, ESD-end systolic dimension, EF-ejection fraction, LA-left atrium dimension, E wave - the maximum speed of the mitral rapid filling, A wave-the maximum rate of mitral late filling. E/A ratio , Sa-systolic mitral annular movement, Ea-early diastolic mitral annular movement , Aa-late diastolic mitral annular movement, ratio E/Ea, relation the maximum speed of the mitral rapid filling vs the maximum speed of the early diastolic mitral annular movement

Table 3. EF frequency.

		Frequency	Percent
Valid	<=45%	32	7.1
	>45%	414	92.2
	Total	446	99.3

Table 4. Influence of EF on dyspnea.

		Sum of Squares	df	Mean Square	F	Sig.
EF	Between Groups	.958	3	.319	4.888	.002
	Within Groups	28.736	440	.065		
	Total	29.694	443			

Table 5. Frequency of diastolic dysfunction.

		Frequency	Percent
Valid	<0.74	146	32.5
	>0.74	293	65.3
	Total	439	97.8

an indicator of asymptomatic diastolic dysfunction, but was increased in patients with systolic heart failure [17].

Methods

The echocardiographic examination was performed on the machine Philips HD 11 probe 2.5 MHz.

The following parameters were obtained by M-mode and 2-dimensional (2D) echocardiography and Doppler echocardiography: end-diastolic and end-systolic dimension of the left ventricle (LV), wall thickness of LV, end-diastolic (EDV), end-systolic (ESV) volumes and LV ejection fraction (EF) were assessed by 2-D echocardiography according to Simpson' method.

Mitral flow was analyzed by pulsed Doppler probe with 2.5 MHz we measured the maximum velocity of mitral flow.

Table 6. Influence of echocardiographyc variables to diastolic dysfunction (E/A < 0.74).

		B	S.E.	Wald	df	Sig.	Exp(B)	95.0% C.I.for EXP(B)	
								Lower	Upper
Step 5(a)	Aa	-1.958	.591	10.990	1	.001	.141	.044	.449
	Ea	1.362	.746	3.335	1	.068	3.905	.905	16.850
	LA	-.040	.017	5.695	1	.017	.961	.930	.993
	Constant	2.473	.675	13.425	1	.000	11.858		

a Variable(s) entered on step 1: LVEDD, LVESD, EF, Aa, Ea, Sa, LA.

Table 7. Frequency of E/Ea ratio HTA patients.

		Frequency	Percent
Valid	≥ 8	335	74.6
	< 8	105	23.4
	Total	440	98.0

Table 8. Influence of LA to E/Ea ratio.

Model	Unstandardized coefficients		Standardized coefficients	t	Sig.
	B	Std. error	Beta		
1 (constant)	14.589	3.215		4.538	.000
LA	-.180	.076	-.113	-2.365	.018

Depended variable E/Ea ratio

Determined by the maximum speed of the mitral rapid filling (E wave) and the maximum rate of atrial contraction (A wave) E/A ratio. Tissue Doppler quantify regional myocardial function analysis of myocardial velocities at four positions of the mitral annulus: septal, lateral, inferior and anterior. Registered as S (maximum speed of positive waves registered in systole), Ea-wave maximum speed registered the rapid charging LV and maximum speed at atrial contraction (Aa). According specifications of Echocardiography Associations of the European Society of Cardiology normal value for Sa and Ea waves is 8 cm/s (less than the average minus two standard deviations), the average value of 12 ± 2 cm/s, depending on age. Determined by the ratio of mitral E wave and Ea (E/Ea) for normal value was considered to be value < 8.

Statistical analysis

In the statistical analysis, descriptive statistic were used, and comparisons were performed for continuous variables by Student's t-test, chi-square test for categorical variables, binary logistic regression and linear regression for calculating the significance of echocardiography parameters to diastolic dysfunction and E/Ea index of HTA patients.

For the calculation of the impacts of certain factors and echocardiography parameters of the diastolic dysfunction was used Pearson´s or Spearman´s correlation. Statistical analysis was performed using the statistical package SPSS 15.0 for Windows. Statistical significance was defined at the level of $p < 0.05$.

Results

The study included 449 patients with hypertension.

Demographic characteristics are on Table 1.

EDD-end diastolic dimension, ESD-end systolic dimension, EF-ejection fraction.

LA-left atrium dimension, E wave - the maximum speed of the mitral rapid filling, A wave-the maximum rate of mitral late filling. E/A ratio, Sa-systolic mitral annular movement, Ea-early diastolic mitral annular movement , Aa-late diastolic mitral annular movement

Index E/Ea, relation the maximum speed of the mitral rapid filling vs the maximum speed of the early diastolic mitral annular movement

Echocardiographic characteristics are on Table 2.

Only 7.1 percent of patients with HTA had EF<45% (Table 3).

Of variable systolic blood pressure, diastolic blood pressure, body mass index (BMI), E/A ratio defined of cut off 0.74, age and EF with cut-off of 0.45, only for symptom dyspnea EF was a considerable (Table 4).

Of HTA patients with calculated E/A ratio , 65.3% had, according to definition, diastolic dysfunction (Table 5).

For the assessment of diastolic dysfunction of the echocardiographic parameters (LVEDD, LVESD, EF, LA, Ea, Aa, Sa), only parameters LA (p=0.017) and Aa (p=0.001) were important (Table 6).

Many HTA patients had E/Ea index ≥8 (Table 7).

On the Table 8 was shown LA influence to E/Ea index.

From age, BMI, duration and height of HTA only duration of HTA have significant correlation with index E/A (p=0.017) (Table 9).

The variables had not significant correlation with ratio E/A (the Table 10).

There were no correlation of ratio E/A with tissue Doppler parameters (Table 11).

Discussion

Ejection fraction

According to data from the Cardiovascular Health Study (CHS) among participants of the study, age ≥65 years showed that subclinical cardiovascular disease (CVD) is very prevalent among older persons, substantially increases the risk of

Table 9. Correlation of E/A ratio with age, BMI, duration and height HTA.

		age	BMI	Duration of HTA	Height of HTA	E/A
age	Pearson Correlation	1	.191(*)	.098(*)	.093	-.013
	Sig. (2-tailed)		.011	.044	.052	.788
	N	448	175	424	439	438
BMI	Pearson Correlation	.191(*)	1	-.050	.135	.053
	Sig. (2-tailed)	.011		.517	.076	.488
	N	175	175	172	173	171
Duration of HTA	Pearson Correlation	.098(*)	-.050	1	.048	.117(*)
	Sig. (2-tailed)	.044	.517		.330	.017
	N	424	172	425	416	416
Height of HTA	Pearson Correlation	.093	.135	.048	1	.084
	Sig. (2-tailed)	.052	.076	.330		.081
	N	439	173	416	439	429
E/A	Pearson Correlation	-.013	.053	.117(*)	.084	1
	Sig. (2-tailed)	.788	.488	.017	.081	
	N	438	171	416	429	439

** Correlation is significant at the 0.01 level (2-tailed). * Correlation is significant at the 0.05 level (2-tailed).

CHD among participants with hypertension or diabetes mellitus [18-19].

Three-quarters of patients with heart failure (HF) has a pre-hypertension (HTA) [20]. Also, HTA plays an important role in HF with preserved EF> 0.50 (HFPEF) [20] In the ALLHAT study, almost half of the patients had HFPEF [21]. The data obtained from this study were : 44% had EF > 0.50; 21% had an EF between 0.40 and 0.50; 17% between 0.30 and 0.40; and 21% with EF <0.30 [20-21]. But studies have shown that patients with EF>0.50 may have reduced left ventricular (LV) contractile function so the hypothesis is not proven that patients EF>0.50 when they had a clear heart failure- pulmonary oedema have transient systolic dysfunction, but for such clinical finding diastolic dysfunction is responsible [22]

Of our patients with hypertension only 7.1% had an EF <45%, but the symptoms of patients with hypertension, that is, dyspnea at rest and exertion were significantly affected only by EF <45%.

Diastolic dysfunction

Doppler measurement are needed to determine hemodynamic state for diastolic dysfunction in addition to measuring the dimensions and volume and calculating EF. [23] Study Ritzema and all showed that direct measurement of the LA pressure (as opposed to pulmonary capillary wedge pressure) noted that the ratio of mitral peak velocity of early filling to early diastolic mitral annular velocity (E/Ea) was the most accurate parameter in the patients with increased LA pressure [24]. Also, in studies it is shown correlation E/E 'with left ventricular filling pressure in patients with atrial fibrillation [25]

In this study, most patients had diastolic dysfunction 65,3 % , two-thirds of patients had E / Ea ≥8 (74.6% of hypertensive patients). We found that LA size has a significant impact on diastolic dysfunction and on ratio E/E' also.

Among the other factors that are significantly correlated with diastolic dysfunction we found-duration of HTA. The data from the other studies showed that diastolic heart failure was more common in elderly [22]. Assessment of LV hypertrophy in patients > 65 and age < 60 age, showed that the elderly patients have greater impairment of LV diastolic function, while the systolic function was preserved, but older patients had pressure load that last longer or the adaptive processes were earlier exhausted [26].The thickness of the septum in hypertensive patients is often associated with the

Table 10. Correlation of E/A ratio with LVEDD, LVESD, EF, thickens of septum, and posterior wall.

		E/A	LV EDD	LV ESD	EF	Thickness of septum	Thickness of p.w.
E/A	Pearson Correlation	1	.022	.045	-.009	-.003	-.010
	Sig. (2-tailed)		.644	.350	.849	.953	.833
	N	439	439	438	438	436	435
LV EDD	Pearson Correlation	.022	1	.510(**)	-.116(*)	.274(**)	.211(**)
	Sig. (2-tailed)	.644		.000	.014	.000	.000
	N	439	447	446	446	444	443
LV ESD	Pearson Correlation	.045	.510(**)	1	-.486(**)	.418(**)	.342(**)
	Sig. (2-tailed)	.350	.000		.000	.000	.000
	N	438	446	446	445	443	442
EF	Pearson Correlation	-.009	-.116(*)	-.486(**)	1	-.030	-.074
	Sig. (2-tailed)	.849	.014	.000		.525	.120
	N	438	446	445	446	444	443
Thickness of septum	Pearson Correlation	-.003	.274(**)	.418(**)	-.030	1	.198(**)
	Sig. (2-tailed)	.953	.000	.000	.525		.000
	N	436	444	443	444	444	442
Thickness of p.w.	Pearson Correlation	-.010	.211(**)	.342(**)	-.074	.198(**)	1
	Sig. (2-tailed)	.833	.000	.000	.120	.000	
	N	435	443	442	443	442	443
LA	Pearson Correlation	-.089	-.020	-.008	-.110(*)	-.036	.010
	Sig. (2-tailed)	.064	.671	.872	.020	.454	.842
	N	437	445	444	444	442	441

Table 11. Correlation of E/A ratio and parameters of tissue Doppler.

		E/A	Ea	Aa	Sa
E/A	Pearson Correlation	1	.056	-.036	-.014
	Sig. (2-tailed)		.390	.580	.829
	N	239	236	.237	231
Ea	Pearson Correlation	.056	1	.838(**)	.643(**)
	Sig. (2-tailed)	.390		.000	.000
	N	236	440	440	433
Aa	Pearson Correlation	-.036	.838(**)	1	.717(**)
	Sig. (2-tailed)	.580	.000		.000
	N	237	440	442	434
Sa	Pearson Correlation	-.014	.643(**)	.717(**)	1
	Sig. (2-tailed)	.829	.000	.000	
	N	231	433	434	434

duration of hypertension, but according to some authors, it is not clear whether it may predict the development of systolic hypertension in healthy individuals [27].

Conclusion

It would be conclude that the diastolic dysfunction occurs in more than half of hypertensive patients, but that the symptoms depend on the ejection fraction, that is the systolic dysfunction responsible for the symptoms. LA size has a significant impact on diastolic dysfunction and index E/Ea, although these echocardiographic changes and diastolic dysfunction were not significantly affected the symptoms of hypertensive patients.

Also duration of hypertension significantly affect diastolic dysfunction.

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