SİSTEMİK ARTERYEL HİPERTANSİYONU OLAN HASTALARDA SOL VENTRİKÜL DOKU DOPPLER GÖRÜNTÜLEME DEĞERLERİ İLE AORTUN ELASTİK ÖZELLİKLERİNİN KARŞILAŞTIRILMASI

Comparison of Left Ventricular Tissue Doppler Imaging Values and Elastic Properties of the Aorta in Patients with Systemic Arterial Hypertension

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ÖZET

Amaç: Hipertansif hastalarda aortik sertlik indeksinin arttığı ve aortik distensibilitenin azaldığı bilinmekte ve bunun kardiyovasküler olay öngördürücüsü olduğu bilinmektedir. Bu çalışmada sistemik arteryel hipertansiyonu (SAH) olan hastalarda sol ventrikül doku doppler görüntüleme (DDG) ile aortun elastik özellikleri arasındaki ilişkiyi saptamayı hedefledik.

Metod: Çalışmaya 18 ile 55 yaş arası izole SAH tanısı almış ek hastalığı olmayan 50 hasta dahil edildi. Hastaların Standart ekokardiyografik parametreleri ölçüldü. Aortik sertlik indeksi (ASİ) ve aortik distensibilite (AD) değerleri hesaplandı. DDG PW eko ile sol ventrikül lateral duvar bazal segmente ait DDG S, E' ve A' hızları, E'/A' oranı ölçüldü.

Bulgular: Hastaların yaş ortalaması 47±7 yıl olup %72'si kadın idi. ASİ ortalama 3.02±0.55 iken AD değeri ortalama 3.93±2.14 [1/(10^3xmmHg)] idi. Ortalama DDG E' ve A' değerleri sırasıyla 9.16±2.35 ve 8.80±2.48 cm/sn olarak bulundu. E'/A' oranı ortalama 1,14±0,47 olup hastaların %44'ünde <1 idi. Yapılan korelasyon analizinde DDG E' dalga hızı azaldıkça ASİ'nin istatiksel olarak anlamlı biçimde arttığı (p<0.001) ve AD'nin ise anlamlı biçimde azaldığı (p<0.001) saptandı. Benzer şekilde E'/A' oranı azaldıkça ASİ'nin anlamlı biçimde arttığı (p<0,001), AD'nin ise anlamlı biçimde azaldığı izlendi (p<0,001)

Sonuç: SAH, sol ventrikülde diyastolik disfonksiyon yaparken eş zamanlı olarak aortda aortik sertliği arttırmaktadır. Bu parametrelerin hipertansif hastanın takibinde ve tedaviye cevabın izlenmesinde kullanılabilir. Bunun için yeni çalışmalara gerek vardır.

Anahtar kelimeler: *Aortik distensibilite; Aortik sertlik indeksi; Diyastolik disfonksiyon; Doku doppler görüntüleme; Hipertansiyon*

ABSTRACT

Objective: Aortic stiffness index is increased and aortic distensibility is decreased in patients with systemic arterial hypertension (SAH) and both of these situations are known as predictors of cardiovascular event. In this study, we searched to detect the correlation between left ventricular diastolic function, measured by tissue doppler imaging (TDI), and elastic properties of the aorta in patients with SAH

Methods: Fifty patients with isolated SAH, age between 18 and 55 years, without any other disease were included in the study. Standart echocardiographic parameters were measured. Aortic stiffness index (ASI) and aortic distensibility (AD) values were calculated. With TDI PW echocardiography S, E', A' velocities and E'/A' ratio of left ventricular lateral wall basal segment were obtained.

Results: Mean age was 47±7 years and 72% of them were female. Mean ASI and AD values were found to be 3.02±0.55 and 3.93±2.14 [1/(10^3xmmHg)] accordingly. Left ventricular lateral wall basal segment mean DDG E' and A' values were found to be 9.16±2.35 and 8.80±2.48 cm/sn accordingly. 44% of patients had E'/A' ratio <1. In the correlation analysis, it was found that ASI increased significantly (p<0.001) and AD decreased significantly (p<0.001) as DDG E' velocity decreased. Similarly, it was observed that ASI increased significantly (p<0.001) and AD decreased significantly (p<0.001) as E'/A' ratio decreased.

Conclusion: Systemic arterial hypertension causes aortic stiffness along with diastolic dysfunction in the LV. These parameters may be used in the follow-up of hypertensive patients and in the assesment of antihypertensive drug therapy. For this purpose, new clinical studies are needed.

Key words: *Aortic stiffness index; Aortic distensibility; Diastolic dysfunction; Tissue Doppler imaging; Hypertension*

INTRODUCTION

Systemic arterial hypertension is defined as blood pressure ≥140 mmHg in systolic and/or ≥90 mmHg in diastolic (1). Affecting nearly one billion people all over the world, systemic arterial hypertension which is a disease easy to diagnose and the most commonly seen cardiovascular risk factors can result in myocardial infarct, stroke, heart failure, atrial fibrillation, aort disection and perivascular artery disease (2).

Since asymptomatic nature of the hypertension, the diagnosis is delayed and necessity of continuous follow-up of medical treatment makes blood pressure control difficult, thus only one of three patients whose blood pressure are under control in accordance with the current guidelines can be protected from end-organ injury such as myocardial infarctus, stroke or heart failure. So blood pressure control should not be the only parameter to decide treatment modification or intensity, besides new parameters are needed to detect end-organ injury at preclinical stage. For this purpose, echocardiography used very fruquently in cardiology practice provides important and prosperious data. Left ventricular mass (LVM), left ventricular mass index (LVMI), left atrial size and volume, left ventricle (LV) diastolic parameters (such as mitral E and A wave, isovolumetric relaxation duration, decelaration time), E' velocity end E/E' ratio of LV mitral lateral annulus by tissue Doppler, carotis intima-media thickness and flow mediated vasodilatation are some of parameters which can be obtained by the help of echocardiography to predict cardiovascular event risk due to atherosclerosis (3, 4, 5). Similary it has been reported that aortic stiffness index (ASI) and aortic distensibility (AD), measured by echocardiography, can be used to predict cardiovascular event risk (6, 7). It is well known that ASI is increased and AD is decreased in the patients with systemic arterial hypertension (8). ASI and AD values can be obtained by echocardiography and pulse wave velocity method (9).

To get knowledge about LV diastolic function, mitral inflow samples are fruquently used. Since they are preload-dependent and can show pseudonormal pattern, they can not reflect diastolic dysfunction totally. However, with tissue Doppler imaging, mitral annulus diastolic longitidunal velocity values are free of preload effect, there is no pseudonormal pattern in which E'/A' ratio is always <1 in case of diastolic dysfunction and additionally the more severe diastolic dysfunction is, the more E' velocity decreases.

Longitidunal mitral annulus diastolic velocities measured via tissue Doppler method are decreased among hypertensive patients as a sign of diastolic dysfunction (10). This situation become more prominent in case of uncontrolled hypertension. It is known that there is strong correlation between level of diastolic dysfuntion and cardiovascular event risk.

In this study, the relation between diastolic function of left ventricle and elastic properties of aorta (aortic stiffness index and aortic distensibility) is searched among patients below 55 years old with isolated systemic arterial hypertension by using echocardiography.

MATERIAL AND METHODS

Fifty patients aged between 18 to 55 years old with systemic arterial hypertesion but without any additional disease were included in the study.

Data related to the disease duration, history of smoking antihypertensive drugs use were recorded. Waist circumference, weight, height of all patients were measured and their body mass index and body surface area (BSA) by using DuBois formula were calculated accordingly (11). To calculate ASI and AD values, during echocardiographic examination, systolic (SBP) and diastolic (DBP) blood pressures were measured with the help of sphygmomanometer and heart rate was obtained from electrocardiographic recording of echocardiography machine simultanously. The difference of SBP and DBP was used as pulse pressure (PP). In echocardiographic examination, LV end-diastolic diameter (LVEDD), LV end-systolic diameter (LVESD), posterior wall diastolic thickness (PWd), interventricular septum diastolic thickness (IVSd) were measured at M-mode images in accordance with the rules set by American Echocardiography Society.

E-IVS distance was measured at mitral valve level and left atrial size (LA) was measured at the level of aortic sinus valsalva level by using M-mode images (12). Fractional shortening (FS) values of the patients are calculated by the machine itself automatically according to the (LVEDD-LVESD)/LVEDD formula. LVM of the patients were obtained by using $0.8x[1.04([LVEDD+PWd+IVSd]^3-[LVESD]^3)]+0.6$ gram formula. LVMI was calculated by dividing LVM into BSA (13).

From the images of apical two- and four-chamber echo windows, LV ejection fractions (LVEF) were obtained by using modified Simpson method and average of two values was determined as LVEF. At apical four-chamber window, by using pulse wave (PW) Doppler, samples of transmitral diastolic inflow were obtained and then mitral E wave, A wave and deceleration time (DT) of E wave were measured. E/A ratios of all patients were calculated. In similar fashion, at apical five-chamber window, isovolumetric relaxation time (IVRT) was obtained. All measurement were carried out at the end of expirium. By using pulse wave tissue Doppler imaging (PWTDI), all diastolic and systolic myocardial velocities were obtained. In this study, to make the evalution simple, sample volum at LV lateral wall basal segment was used to obtain E' wave, A' wave and S wave velocities at apical four-chamber window. E/E' ratios were calculated accordingly. All Doppler measurements were carried out for the five subsequent cycles and the average of all five measurements were used for statistical analysis.

Following the echocardiographic examination of heart, at parasternal long axis M-mode images, the systolic (Asd) and diastolic (Add) aortic diameters of ascending aorta from lower margin of upper wall to upper margin of lower wall were measured 3 cm distal to the aortic valve level, discriminating diastole and systole by using simultaneous ECG recordings. While aortic stiffness index is calculated by using ASI= ln(SBP/DBP)/[(Asd-Add)/Add] formula, aortic distensibility is obtained by using $AD[1/(10^3 xmmHg)] = 2x\ [(Asd-Add)/Add]/PP$ formula (14).

Statistical Analysis

Statistical analysis was carried out by using SPSS 11.5 (Statistical Package for Socia Sciences-SPSS, Inc., Chicago, Illnois, USA) programe. While categorized variables were expressed as percentage, continuous variables were expressed as arithmetic average ± standart deviation (SD). One-Sample Kolmogorov-Smirnov test was applied to check whether continuous variables were distributed normally. All continuous variables of the study were normally distributed. Possible associations between continuous variables were analysed by using Pearson correlation test. Possible statistical difference between group characteristics was analysed by using Student's t test. p value <0.05 was considered statistically significant.

RESULTS

Fifty patients were included in the study with avarage age of 47±7 years and 36 of them were women. Demographic and clinical characteristics of the patients are shown at Table 1.

Table 1. Demographic and clinical characteristics of the patients

	n=50
Age (year)	47± 7
Gender (Fermale/Male) (%)	36/14(72/28)
Height (cm)	162±8
Body weight (kg)	78±12
Body surface area (m^2)	1,89±0,18
Waist Cicumference (cm)	
Female	96±11
Male	100±9
Body Mass Index (kg/m^2)	29,5±4,5
Smoking cigarette (%)	9 (18)
Type of medication	
ACEI (%)	3(6)
ACEIve tiazide (%)	14 (28)
ARB (%)	3 (6)
ARB ve tiazide (%)	12 (24)
CCB (%)	13 (26)
β-Blocker (%)	10 (20)
Alfa-receptor blockers (%)	1 (2)
Life style changes (%)	12 (24)
SBP (mmHg)	125±18
DBP (mmHg)	75±8
Hipertension duration (year)	4,6±3,7
Heart rate (beat/minute)	75±9

Echocardiographic examination results of the patients are presented at Table 2.

Average ASI and AD values which are parameters expressing the elastic properties of the aorta, were 3.02±0.55 and 3.93±2.14 [1/(10^3xmmHg)] accordingly. All the TDI measurements, aortic diameters, ASI and AD values were shown at Table 3. There is no standart, commanly agreed upper and lower limit values for ASI and AD, if it is assumed that 3.0 and below is normal for ASI, 44% of patients (n=22) had normal ASI value. Similarly if it is assumed that 4 [1/(10^3xmmHg)] and above is normal for AD, 42% of patients had normal AD values. According to these assumptions, there was only one patient who has normal AD value but high ASI value. Fifty two percent of the patients had E/A ratio <1 and so relaxation type diastolic dysfunction. Only two patient had pseudonormal patern which is E/A ratio of >1, DT of >160 seconds and E'/A' ratio of <1. Rest of the patients had normal diastolic dysfuntion.

Table 2. Basal echocardiographic examination results of the patients.

	n=50
FS (%)	37±3
E-IVS distance (cm)	0,53±0,13
LVEF (%)	67±3
LVEDD (cm)	4,70±0,45
LVEDD (cm/m²)	2,50±0,35
LVESD (cm)	2,99±0,34
LVESD (cm/m²)	1,59±0,20
Right ventricular diameter (cm)	2,52±0,24
Right ventricular diameter (cm/m²)	1,34±0,13
Left atrium diameter (cm)	3,91±0,33
Left atrium diameter (cm/m²)	2,07±0,15
IVSd (cm)	1,05±0,18
PWd (cm)	0,96±0,11
LV mass (gram)	
Female	162±34
Male	182±34
LVMI (gr/m²)	
Female	89±18
Male	93±20
Mitral E wave (cm/second)	67±16
Mitral A wave (cm/second)	64±14
Mitral E/A ratio	1,09±0,33
Decerelation Time (milisecond)	195±32
IVRT (milisecond)	79±16

Table 3. Echocardiographic examination results of the patients showing TDI measurements, aortic diameters and aortic elastic properties

	n=50
Aortic systolic diameter (cm)	3,09±0,34
Aortic diastolic diameter (cm)	2,84±0,35
Aortic stiffness index	3,02±0,55
Aortic distensibility [1/(10^3xmmHg)]	3,93±2,14
LV lateral wall basal segment S wave (cm/sn)	7,26±1,28
LV lateral wall basal segment E' wave (cm/sn)	9,16±2,35
LV lateral wall basal segment A' wave (cm/sn)	8,80±2,48
LV lateral wall basal segment E'/A' ratio	1,14±0,47
Left ventricule E/E' ratio	7,59±2,21

Correlation analysis was carried out between diastolic function parameters and elastic properties of aorta, the results were shown at Table 4.

In statistical analysis, it was found that the more TDI E' wave value decreases, the more ASI value increase significantly (r value -0.499, p<0.001) and similarly the more aortic distensibility decreases significantly (r value 0.477, p<0.001). There was no statistical correlation between left ventricule E/E' ratio and aortic elastic properties significantly. On the other hand, it was found that the more E'/A' ratio increases, the more ASI value decreases significantly (r value -0.696; p<0.001) and similarly the more AD value increases significantly (r value 0.691; p<0.001). All results of correlation analysis between LV lateral wall basal segment TDI values and elastic properties were shown at Table 5.

Table 4. The statistical relation between basic echocardiographic results and TDI E' wave, E'/A' ratio, aortic elastic properties of the patients.

	ASI		AD		E'/A'		TDI E'	
	r	**p**	**r**	**p**	**r**	**p**	**r**	**p**
IVSd	0.372	0.008	-0.454	0.001	-0.323	0.022	-0.385	0.006
PWd	0.392	0.005	-0.387	0.006	-0.308	0.030	-0.423	0.002
LVMI	0.624	0.000	-0.585	0.000	-0.617	0.000	-0.588	0.000
LAD	0.546	0.000	-0.443	0.001	-0.422	0.002	-0.380	0.007
Mit.E	-0.454	0.001	0.404	0.004	0.581	0.000	0.487	0.000
Mit.A	0.478	0.000	-0.496	0.000	-0.461	0.001	-0.306	0.031
DT	0.444	0.001	-0.358	0.011	-0.331	0.019	-0.174	0.226
IVRT	0.460	0.001	-0.438	0.001	-0. 553	0.000	-0.466	0.001
E/A	-0.715	0.000	0.710	0.000	0.848	0.000	0.638	0.000

Table 5. The statistical relation between aortic elastic properties and TDI measurements

	ASI		AD	
	r	**p**	**r**	**p**
TDI S velocity	-0.168	0.244	0.061	0.676
TDI E' velocity	-0.499	0.000	0.477	0.000
TDI A' velocity	0.588	0.000	-0.561	0.000
E'/A' ratio	-0,696	0,000	0,691	0,000

DISCUSSION

Aortic stiffness increases not only in case of hypertension but also increases in case of atherosclerosis, aging, diabetes mellitus, chronic kidney failure (6, 7, 8). It is an independent marker for cardiovascular event and stroke risk in hypertensive patients (9). Thus, increase in ASI and decrease in AD are expected result for hypertensive patients who have diastolic dysfunction at the same time (15).

In the literature, there are studies comparing the diastolic dysfunctions with elastic properties of aorta and studies about elastic properties of aorta measured by the help of pulse wave velocity method (16, 17). In this study, instead of PWV method; echocardiographic method was used to evaluate elastic properties of aorta (14). To reduce the effect of age on aortic stiffness, population of the study was composed of young patients with average age of 47±7 years. By this privilage, the effect of hypertension on aortic elastic properties become more prominent in the study.

In the analysis, it was found that parellel to the decrease in myocardial TDI E'/A' ratio there is statistically significant increase in ASI ($p<0.001$) and decrease in AD ($p<0.001$). Compared to the patients with E'/A' ratio ≥1; the patients with E'/A' ratio <1 had significantly higher ASI values (average values 3.38±0.48 vs 2.74±0.42 with 95% CI $p<0.001$ accordingly) and lower AD values (average values 2.67±1.67 vs 4.91±1.95 with 95% CI $p<0.001$ accordingly). All these results shows that diastolic dysfunction goes along with changes in aortic elasticity. Similarly Mottram et al. found that aortic complience is independent predictor of diastolic dysfunction (15). To explain this, some mechanisms can be offered. Increase in aortic stiffness results in increase in velocity of blood flow passing through aorta and LV ejection, this leads early return of reflecting waves at systole and it ends up with increase in LV afterload (18).

Increased afterload causes myocyte hypertrophy and decreased LV relaxation (19). Simultaneously, decreased DBP leads decrease in coronary perfusion and together with hypertrophy it causes subendocardial ischemia. All of them viciously impair LV relaxation more (20). Thus not only hypertension itself, but also aortic stiffness itself increases diastolic dysfunction and contributes the continuity of diastolic dysfuntion.

Left ventricle E/E' ratio is one of indicators of diastolic dysfunction, and the value increases as the severity of diastolic dysfunction increases and it is well correlated to left ventricle end diastolic pressure. Decrease in aortic complience and increase in E/E' ratio has been shown to be well correlated (15). In our study, although there was tendency of increasing in ASI value and decreasing in AD value as E/E' ratio increase, the relation between them was not statistically significant. Possible reason for this result can be due to low average of E/E' ratio (average value 7.59±2.21) for the study population, in other words, the number of people with severe diastolic dysfunction was too low for statistical analysis. Only two patients had pseudonormal pattern, bu none of them had restrictive diastolic dysfunction.

Left ventriclar hypertrophy (LVH) and arterial stiffness mostly result from structural changes. In both clinical situations, hypertension itself cause increase in the activation of renin-angiotensin-aldosteron system, sympathetetic system and growth factors and those factors lead extracellular matrix accumulation, fibroblast proliferation, vascular smooth muscle and myocyte hypertrophy in related structures. Those changes become permanent in case of uncontrolled blood pressure. Positive effect of the treatment on hemodynamic changes (such as reversal of diastolic dysfunction) is seen earlier, but histopathological changes of left ventricle or reversal of aortic elasticity need longer duration. For example, in LIFE study, LV hypertrophy reduced significantly after one-year treatment for hypertension (21). Similarly Çelik et al. found positive effect of the treatment on arterial stiffness just after 6. month (22). So it is well expected that structural changes such as LV hypertrophy and arterial stiffness take place long after the development of diastolic dysfunction and after the treatment is started the diastolic dysfunction reverse firstly. Results of our study also support these findings. Although 26 patients had diastolic dysfunction only 15 of them had LV hypertrophy. All the patients with LVH had diastolic dysfunction as expected.

Major limiting factors of the sudy are usage of only LV lateral wall basal segment TDI values, limited number of patients with severe diastolic dysfunction (pseudonormal or restrictive type), lack of ruling out possibility of asympthomatic atherosclerosis.

In conclusion; aortic stiffness increases and aortic distensibility decreases among hypertensive patients with diastolic dysfuntion accordingly. Additional to the standart Doppler measurement, tissue Doppler imaging has continuous relation with diastolic dysfuntion without showing pseudonormal pattern. TDI measurements correlated well with ASI and AD.

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