Effect of lifestyle modifications on diastolic functions and aortic stiffness in prehypertensive subjects: a prospective cohort study

Prehipertansif bireylerde yaşam şekli değişikliğinin diyastolik fonksiyonlar ve aort sertliği üzerine etkisi: İleriye dönük bir kohort çalışma

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Abstract

Objective: Prehypertension is one of the primary causes of major cardiovascular events independent from other cardiovascular risk factors. The aim of the study was to evaluate the effect of therapeutic lifestyle modifications (LSMs) on cardiac diastolic function and aortic stiffness in prehypertensive subjects.

Methods: This study designed as a prospective cohort study. Sixty-one prehypertensive adults were included in this study. The goals of LMS were weight loss of at least 5 kg in subjects with a BMI $\geq$25 kg/m^2 and moderate-intensity physical activity at least 180 minutes per week. We evaluated left ventricular (LV) diastolic function and aortic stiffness parameters at baseline and after 6 months by conventional and tissue Doppler imaging (TDI) echocardiography. Statistical analyses were performed using Wilcoxon-signed rank test and the paired sample t test.

Results: Transmitral early velocity (E), the ratio of E to transmitral late velocity (E/A), TDI diastolic early septal velocity (septal E), TDI systolic septal velocity (septal S), TDI early lateral velocity (lateral E), the ratio of septal E to TDI late septal (septal A) velocity (septal E/A) and the ratio of lateral E to late lateral (lateral A) velocity (lateral E/A) were found to be significantly increased after the LSMs ($p<0.05$ for all). The beta stiffness index was decreased (12.07 vs. 6.33; $p < 0.001$) and the aortic compliance (0.02 cm/mmHg vs. 0.05 cm/mmHg; $p<0.001$) and the aortic strain (3.28% vs. 7.02%; $p<0.001$) were increased significantly after the LSMs.

Conclusion: LSMs improve conventional and TDI echocardiographic parameters and aortic stiffness measurements in subjects with prehypertension. *(Anadolu Kardiyol Derg 2013; 13: 446-51)*

Key words: Prehypertension, Doppler echocardiography, aortic stiffness, life change events

ÖZET

Amaç: Prehipertansiyon, diğer kardiyovasküler risk faktörlerinden bağımsız olarak majör kardiyovasküler olayların primer nedenlerinden biridir. Terapotik yaşam şekli değişikliğinin prehipertansif bireylerde kardiyak diyastolik fonksiyonlar ve aort sertliği üzerine etkisini değerlendirdik.

Yöntemler: Prospektif kohort olan bu çalışmaya 61 prehipertansif birey alındı. Katılımcıların hedefi vücut kitle indeksinin 25 kg/m^2 ve üzerinde olanlarda en az 5 kg kilo kaybı ve haftada en az 180 dakika orta-ileri düzeyde fiziksel aktivite yapmaları idi. Çalışma başlangıcında ve 6 ay sonra konvansiyonel ve doku Doppler ekokardiyografi ile sol ventrikül diyastolik fonksiyon ve aort sertliği parametrelerini değerlendirdik. İstatistiksel analiz olarak Wilcoxon-signed rank testi ve eşleştirilmiş t testi ile analiz edildi.

Bulgular: Transmitral erken akım hızı (E), E/A oranı, septal E, septal S, lateral E, septal E/A oranı ve lateral E/A oranı yaşam biçimi düzenlemesi ile anlamlı olarak arttı (tüm değişkenler için $p<0{,}05$). Beta sertlik indeksi azaldı (12,07 ve 6,33; $p<0{,}001$), aort kompliyansı (0,02 cm/mmHg ve 0,05 cm/mmHg; $p<0{,}001$) ve aort gerilebilirliği (%3,28 ve %7,02; $p<0{,}001$) bazale göre arttı.

Sonuç: Prehipertansif bireylerde yaşam şekli düzenlenmesi konvansiyonel ve doku Doppler ekokardiografik parametreleri ve aort sertliği ölçümleri üzerine düzeltici etkiler yapmaktadır. *(Anadolu Kardiyol Derg 2013; 13: 446-51)*

Anahtar kelimeler: Prehipertansiyon, Doppler ekokardiyografi, aort sertliği, yaşam değişikliği olayları

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Introduction

Prehypertension is associated with an increased risk of major cardiovascular events independently of other cardiovascular risk factors (1). The Seventh Report of the Joint National Committee (JNC) on Prevention, Detection, Evaluation and Treatment of High Blood Pressure defined blood pressure (BP) levels of 120 to 139/80 to 89 mm Hg as prehypertension and those of ≥140/90 mm Hg as hypertension (2). The population-attributable fraction of prehypertension was 13.2% in a general population, which was similar to those of stages 1 and 2 hypertension (3). It has been shown that lifestyle modifications (LSMs) decrease the progression of hypertension and cardiovascular end-organ damage in individuals with prehypertension (4, 5). Some left ventricular (LV) diastolic parameters such as the ratio of early to late transmitral peak velocities (E/A ratio), tissue Doppler imaging (TDI) mitral annular velocity (Ea) and the ratio of transmitral early velocity to tissue Doppler mitral annular velocity (E/Ea) have been reported to be impaired in subjects with prehypertension (6). It has also been demonstrated that aortic elasticity is impaired in young patients with prehypertension compared with healthy controls (7) and that impaired arterial stiffness is significantly associated with the markers of inflammation in patients with prehypertension (8).

Many studies have investigated the effects of the LSMs on cardiovascular risk in prehypertensives (5, 9, 10). Aizawa et al. (11) have found that LSMs improve carotid artery stiffness in metabolic syndrome subjects with prehypertension and prediabetes. However, there are no studies on the effect of LSMs on LV diastolic functions and aortic stiffness.

The main objective of this study was to interpret the effect of therapeutic lifestyle modifications (LSMs) on cardiac diastolic function and aortic stiffness in prehypertensive subjects.

Methods

Study design

A prospective cohort study.

Study population

The study was conducted in our cardiology clinic. Participants enrolled in the study were selected among healthy people who were admitted to the Namık Kemal University and who agreed to participate in the study between March 2010 and November 2011. Inclusion criteria were systolic blood pressure (BP) of 120-139 mmHg and/or diastolic BP of 80–89 mmHg. Patients with known atherosclerotic cardiovascular disease, aortic diseases, arrhythmia, valvular heart disease, diabetes mellitus, and chronic inflammatory disease were excluded. We enrolled 72 subjects with prehypertension. Eleven subjects did not coordinate to LSMs, so this prospective study was conducted on 61 prehypertensive adults aged 30-65 years (33 men and 28 women).

All the participants had signed an informed consent form, and the protocol of the study was approved by the local ethics committee.

Intervention

Right-and left-arm BP values of all participants were recorded. Resting BP(5 minutes after resting) was measured at three different times and 120-139/80-89 mmHg of systolic and diastolic values were diagnosed as prehypertension.

Therapeutic LSM is the lifestyle component of the Third Report of the NCEP Adult Treatment Panel (ATP) III guidelines (12). It focuses on diet, including low salt and calorie restriction under the control of a dietician, weight management and increased physical activity. The participants' goals were weight loss of at least 5 kg in subjects with a body mass index (BMI) of 25 kg/m^2 or greater, at least 180 minutes per week of moderate-intensity physical activity, no more than 100 mmol/day of dietary sodium and a reduction in alcohol consumption (<30 mL/ day for men and <15 mL/ day for women). Participants enrolled in the study also received counseling on the DASH diet, including advice about increased consumption of fruits and vegetables (9 to 12 servings/d) and low-fat dairy products (2 to 3 servings/d) and reduced consumption of saturated fat (7% of energy) and total fat (25% of energy) (4).

Study protocol

In addition to BP, the subjects' height, weight, BMI, fasting blood glucose, serum lipids, lipoproteins, diastolic function and aortic stiffness parameters were evaluated both at baseline and 6 months after the commencement of the LSMs. The patients did not use any antihypertensive drugs during the study period.

Echocardiographic examination

All the participants underwent a complete transthoracic echocardiographic examination: this included two-dimensional, pulsed-wave Doppler transmitral recordings and TDI recordings of mitral annulus diastolic velocities using a 3.5-MHz sector transducer (Esaote My Lab 50, Genua, Italy). Two-dimensional and pulsed-wave Doppler echocardiographic studies were performed in the left lateral decubitus position with conventional views (parasternal long- and short-axis, apical 4-chamber). An electrocardiogram was recorded simultaneously with its tracings on the M-mode or Doppler monitor. M-mode measurements were used according to the recommendations of the American Society of Echocardiography (13).

Mitral inflow velocity was recorded from the apical 4-chamber view by pulsed-wave Doppler sampling during diastole. Peak early (E) and late (A) mitral inflow velocity, the E/A ratio and the deceleration time of the E velocity (DT) were obtained. The LV ejection time (LVET) was measured from the onset to the end of the LV outflow. The isovolumetric relaxation time (IVRT) of the LV was obtained as the time interval from the cessation of LV outflow to the onset of mitral valve inflow. The isovolumetric contraction time (IVCT) of the LV was the interval from the cessation of mitral inflow to the onset of LV outflow. TDI of the mitral annulus velocities was applied at the septal and lateral sides with the same echocardiographic unit in the pulsed-Doppler mode, and systolic (septal S and lateral S), early diastolic (septal E and lateral E), late diastolic (septal A and lateral A) velocities and E/A

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Table 1. Basal characteristics of prehypertensives

Variables	Value
Gender, male/female	33/28
Age, years	47.8±7.1
Smoking, yes/no	18/43
Height, cm	166.41±8.02
Weight, kg	84.08±18.71
Body mass index, kg/m^2	29.3±4.9
Waist circumference, cm	99.6±11.1
SBP, mmHg	132.8±5.10
DBP, mmHg	83.9±4.5

The data are presented as mean±standard deviation and numbers
DBP - diastolic blood pressure, SBP - systolic blood pressure

ratios were measured. A mean of three consecutive cycles was used to calculate all echocardiographic measurements and then averaged. We used E/A ratio, DT and IVRT as conventional and septal E/septal A, lateral E/lateral A, E/septal E, E/lateral E as tissue Doppler echocardiographic parameters for diastolic function.

Guidelines and Standards of American Society of Echocardiography recommends (14) the normal values of diastolic function parameters according to age groups. Because the subjects in our study have wide range aged, we planned this study as values of baseline and six month later.

Measurement of the aortic elasticity parameters

BP was recorded using a standard sphygmomanometer cuff from the right arm during the echocardiographic examination. Echocardiographic recordings were performed, and the average of three consecutive cycles for each parameter was calculated. A clear image of the proximal aorta was acquired in the parasternal long axis view, showing the position of the right coronary and the noncoronary valve. An M-mode bar was placed 3 cm over the aortic valve coaptation line for measurement of the systolic and diastolic diameters of the ascending aorta. The systolic diameters were measured at the maximum anterior systolic aortic movement, and the diastolic diameters were measured at the peak of the QRS complex on the simultaneously recorded ECG. Aortic stiffness was measured according to the following formulas (15):

Aortic compliance (cm/mmHg)=systolic diameter-diastolic diameter/systolic pressure-diastolic pressure

Aortic strain %=[systolic diameter-diastolic diameter (ΔD) / diastolic diameter (D)]x100

Beta (stiffness) index=ln (Systolic pressure/diastolic pressure)xD/ΔD

To avoid any bias, the echocardiographic measurements were acquired by one cardiologist, and the repeated images were also analyzed by another cardiologist blinded to the clinical details.

Statistical analysis

Statistical analysis was performed with SPSS for Windows version 17.0 (SPSS Inc., Chicago, IL, USA).The Kolmogorov-Smirnov test used for normality test. The data are presented as median with data range (minimum to maximum) for without normal distribution. The data are presented as mean±standard deviation for normal distribution. Nonparametric continuous variables were tested with the Wilcoxon - signed rank test. Variables with normal distribution were analyzed with the paired sample t test. A p value of <0.05 was considered to indicate statistical significance.

Results

The changes in physical and metabolic parameters after the LSMs

The basal characteristics of study population are shown in Table 1. The changes in metabolic parameters after the LSMs are shown in Table 2. Heart rate (p=0.001), systolic BP (p=0.001), diastolic BP (p=0.001) and waist circumference (p=0.017) were significantly decreased after the LSMs. Glucose (p=0.015), uric acid (p=0.049) and triglyceride (p=0.031) were significantly decreased after the LSMs.

Weight, BMI, total cholesterol and low-density lipoprotein cholesterol levels decreased after LSM, but these changes were not statistically significant. High-density lipoprotein cholesterol levels increased after the LSMs, but the changes was not statistically significant.

Diastolic function parameters after the LSMs

Transmitral E velocity (p<0.001) and E/A ratio (p<0.001) were significantly increased after the LSMs. The IVRT (p<0.001) and DT (p<0.001) were significantly decreased after the LSMs compared with the baseline values, whereas the transmitral A wave velocity, IVCT and ET remained unchanged (Table 3).

On the other hand, we observed significant changes among the TDI measurements. The septal E (10 cm/s vs. 11 cm/s; p=0.014), septal S (9 cm/s vs. 10 cm/s; p=0.05), lateral E (11.3 cm/s vs. 12.4 cm/s; p=0.01), septal E/A ratio (0.99 vs. 1.15; p=0.003) and the lateral E/A ratio (1.14 vs. 1.30; p=0.008) were significantly increased after LSM, but the septal A (10.7 cm/s vs. 9.9 cm/s; p=0.05) was significantly decreased after the LSMs. However, the changes in lateral A, lateral S, E/septal E and E/lateral E variables were not statistically significant (Fig. 1).

Aortic stiffness parameters after the LSMs

We observed a significant change among aortic stiffness measurements. The beta stiffness index was decreased (12.07 vs. 6.33; p<0.001) and the aortic compliance (0.02 cm/mmHg vs. 0.05 cm/mmHg; p<0.001) and the aortic strain (3.28% vs. 7.02%; p<0.001) were increased significantly after the LSMs (Fig. 2).

Discussion

Our results suggested that the LSMs not only decrease the BP, waist circumference, glucose, uric acid and triglyceride levels, but also improve the diastolic function and aortic stiffness parameters.

Table 2. Demographic and laboratory characteristics before and after lifestyle modifications in prehypertensives

Variables	Before	After	*p
Heart rate, beats/min	76 (60-95)	74 (60-90)	<0.001
SBP, mmHg	132.8±5.10	117.6±7.02	<0.001
DBP, mmHg	84 (70-89)	76 (70-80)	<0.001
Body mass index, kg/m^2	29.7 (19.8-40.4)	28.8 (19.2-35.9)	NS
Waist circumference, cm	99.6 (76-125)	97.4 (76-120)	0.017
Glucose, mg/dL	93 (69-124)	89 (70-124)	0.015
Uric acid, mg/dL	4.8 (2-7)	4.6 (2.5-6)	0.049
Total cholesterol, mg/dL	201(140-267)	196.8 (158-242)	NS
Triglyceride, mg/dL	157.74±51.78	148.87±35.76	0.031
HDL, mg/dL	44.8 (22-81)	45.6 (35-63)	NS
LDL, mg/dL	138.45±21.66	131.65±25.03	NS

The data are presented as mean±standard deviation and median (minimum to maximum) values.
*Wilcoxon - signed rank test and paired sample t test
DBP - diastolic blood pressure, HDL - high-density lipoprotein, LDL - low-density lipoprotein, NS - statistically no significant, SBP - systolic blood pressure

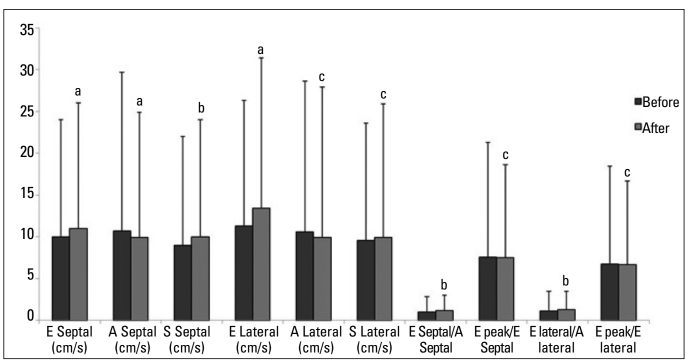

Figure 1. TDI measurements before and after lifestyle modifications in prehypertensives
E septal ($^a p < 0.05$), S septal ($^b p < 0.01$), E lateral ($^a p < 0.05$), E septal /A septal ratio ($^b p < 0.01$) and E lateral /A lateral ratio ($^b p < 0.01$) were significantly increased after lifestyle modification. ^{c}NS

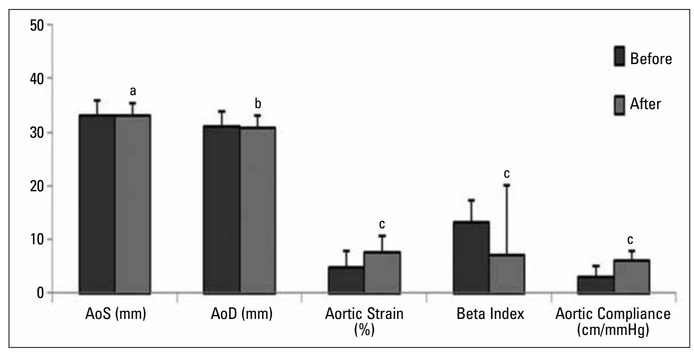

Figure 2. Aortic stiffness measurements before and after lifestyle modifications in prehypertensives
Aortic diastolic diameter (AoD) ($^b p<0.05$), beta stiffness index was decreased ($^c p<0.001$). Aortic compliance ($^c p<0.001$) and aortic strain (%) ($^c p<0.001$) were higher than baseline. Aortic systolic diameter (AoS) did not change. Aortic compliance values are shown multiplied by 100

Based on new data on the lifetime risk of hypertension, the JNC 7 report (2) has introduced a new classification that includes the term 'prehypertension' for those with systolic BP ranging from 120 to 139 mmHg and/or 80 to 89 mmHg diastolic BP. This new designation is intended to identify those individuals in whom early intervention by adoption of healthy lifestyles could reduce BP, decrease the rate of progression of BP or prevent hypertension entirely. Multiple lifestyle factors, such as physical inactivity, excessive intake of calories, sodium, saturated fat, and cholesterol and an inadequate intake of fruits, vegetables and low-fat dairy products are etiologically related to the development of atherosclerotic cardiovascular disease, overweight and obesity, elevated BP and lipid levels and diabetes (12).

Prehypertension appears to be associated with an increased risk of myocardial infarction and coronary artery disease (CAD) but not stroke (16). Lifestyle measures, such as weight reduction, regular exercise and a low-salt diet, have been shown to lower BP and to reduce the risk of progression to hypertension (17-19). A number of studies have shown the effect of such modification on certain components of cardiovascular risk (18, 20). In obese and overweight persons, weight reduction, a low-sodium DASH-type diet and physical activity are all useful in the prevention of high BP and the reduction of cardiovascular risk (5). In our study, the prehypertensive subjects participated in therapeutic LSMs for 6 months. Our results showed that the subjects who enacted lifestyle changes experienced a reduction in BP and waist circumference and a reduction in glucose, uric acid and triglyceride levels. Weight, body mass index, total cholesterol and low-density lipoprotein cholesterol levels decreased after LSM, but these were statistically not significant. High-density lipoprotein cholesterol levels increased after the LSMs but were also statistically not significant. This may be due to the small number of subjects or the short duration of the study.

The most interesting finding obtained from this study that LSMs improves in some diastolic function and aortic stiffness parameters compared to the previous values in subjects with prehypertension. The diastolic functions were evaluated by conventional Doppler and TDI in prehypertensive subjects

Table 3. M-mode and pulsed-Doppler indices before and after lifestyle modifications in prehypertensives

Variables	Before	After	*p
Left atrium diameter, mm	34 (28-44)	33.8 (4.4-4.3)	NS
LVDD, mm	45 (40-56)	45 (7-56)	NS
LVSD, mm	29 (24-36)	30 (23-37)	NS
Interventricular septum, mm	11 (8-15)	11 (9-14)	NS
Posterior wall, mm	11 (9-14)	11 (9-14)	NS
Ejection fraction, %	65 (57-73)	65 (57-73)	NS
E peak, cm/s	73.87±16.26	80.81±12.32	0.001
A peak, cm/s	73.82±14.68	70.30 ± 11.52	NS
E/A ratio	0.90 (0.53-2.19)	1.16 (0.76-1.66)	<0.001
DT, ms	198.63±35.49	168.76±26.69	<0.001
IVRT, ms	101 (63-139)	95 (76-121)	<0.001
IVCT, ms	69.37±9.23	67.85±9.22	NS
ET, ms	285 (220-361)	280 (212-363)	NS

The data are presented as mean±standard deviation and median (minimum to maximum)

*Wilcoxon - signed rank and paired sample t test.

DT - deceleration time, ET - ejection time, IVCT - isovolumic contraction time, IVRT - isovolumetric relaxation time, LVDD - left ventricular diastolic diameter, LVSD - left ventricular systolic diameter, NS - statistically not significant

before and after the LSMs. While the E peak and the E/A significantly increased after the LSMs, the IVRT and DT significantly decreased after the LSMs compared with baseline values in the conventional Doppler examination. In addition, the transmitral A wave velocity, IVCT and ET remained unchanged. We observed a significant change among the TDI measurements. Although the septal E, septal S, lateral E, septal E/A ratio and lateral E/A ratio significantly increased, the septal A ratio significantly decreased after the LSMs. However, the lateral A, lateral S, E/septal E and E/lateral E showed no change. Conventional Doppler and TDI parameters of diastolic function were improved after the LSMs.

Mogelvang et al. (21) revealed that TDI may be helpful in the early identification and follow-up of persons with an increased risk of cardiovascular events and prehypertension with impaired LV function.

Hemodynamic conditions may not be identical at baseline and six months later of LSMs or the parameters of diastolic function and aortic stiffness. E/lateral E and E/septal E amongst of diastolic parameters less affect from load conditions, which they don't affect in this study. These results show that LSMs may have effect by reducing blood pressure, not direct effect on diastolic functions.

Previous work has shown that hypertension decreases aortic strain and distensibility and increases aortic stiffness and that there is an association between aortic stiffness and diastolic dysfunction (22). Research has also shown that young patients with prehypertension have impaired aortic elasticity compared with healthy controls (7) and that they have increased markers of inflammation, namely, hs-C-reactive protein and white blood cell count, compared with controls. Moreover, impaired arterial stiffness has been shown to be significantly associated with the markers of inflammation in patients with prehypertension (8). It is accepted that aortic stiffness is an important factor in the development of atherosclerotic disease. Increased aortic stiffness serves as a stimulus of LV hypertrophy and can reduce coronary artery perfusion (promoting subendocardial ischemia) (23). Stiffening of the aorta increases the LV after load and serves as a potent stimulus for LV hypertrophy. In fact, increased aortic stiffness is an independent predictor of adverse cardiovascular events, even after accounting for the Framingham risk score (23, 24). A decrease in aortic stiffness is seen as an important parameter in the evaluation of treatment success in patients with cardiovascular risk. Both invasive and non-invasive assessments of aortic elasticity are possible. We used non-invasive measurements of the elasticity of the arteries to determine the aortic diameter changes during systole and diastole (25). We observed a significant change among aortic stiffness measurements. The beta stiffness index was decreased; the aortic compliance and the aortic strain were increased significantly after the LSMs.

Our findings suggest that the development of prehypertension may be prevented or delayed by making lifestyle changes, which have the ability to reduce arterial stiffness.

Study limitations

The main limitations of this study are 1) Coronary arteriography was not performed for all the patients. However, a medical history was taken, and physical and electrocardiographic examinations were performed in all the subjects to exclude any CAD. 2) Which ones improve firstly? Aortic stiffness measurements or diastolic function parameters. Perhaps, firstly, blood pressure decreased, subsequently aortic stiffness and diastolic function. We could have verified by serial follow-up examination. 3) We have not control group.

Conclusion

The principal findings of this study are 1) LSMs affect mitral inflow measurements in prehypertensives, 2) some tissue Doppler parameters (septal E, septal E/A, septal S, lateral E and lateral E/A) are improved in prehypertensives after LSMs and 3) aortic stiffness measurements are improved in prehypertensives after LSMs.

We found that the LSMs improved the diastolic function and the aortic stiffness in subjects with prehypertension. However, further studies with longer follow-up period including more subjects are needed to confirm these findings.

Conflict of interest: None declared.

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