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The Relationship between Non-Dipper Blood Pressure and Thoracic Aortic Diameter in Metabolic Syndrome

Metabolik Sendromda Torasik Aort Çapları ile Non-Dipper Kan Basıncı Arasında İlişki

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Abstract

Objective: Non-dipper hypertension is associated with increased cardiovascular morbidity and mortality. The purpose of this study was to evaluate the association of non-dipping hypertension with aortic diameter in patients with metabolic syndrome.

Materials and Methods: This study included 70 hypertensive patients with metabolic syndrome. These patients were evaluated with 24-h blood pressure Holter monitoring and divided into two groups of 35 patients each. Aortic diameter was measured by M-mode and two-dimensional echocardiography. These parameters were compared between the two groups.

Results: In the dipper group, there were 26 female and 9 male patients with a mean age of 55±11 years. In the non-dipper group, there were 25 female and 10 male patients with a mean age of 56±11 years. No significant difference was found between the two groups in terms of basic characteristics. Non-dipper hypertensive patients had a higher thoracic aortic diameter value than dipper patients (35.6±2.4 and 33.23±1.1, p<0.01).

Conclusion: These findings suggest that thoracic aortic diameter value is higher in patients with non-dipper hypertension.

Key Words: Blood pressure, metabolic syndrome, aortic diameter, echocardiography, non-dipper

Özet

Amaç: Non-dipper hipertansiyon artmış kardiyovasküler mortalite ve morbidite ile ilişkilidir. Bu çalışmanın amacı metabolik sendromlu hastalarda aort çapı ile non-dipping hipertansiyon ilişkisini değerlendirmektir.

Gereç ve Yöntem: Çalışmaya metabolik sendromlu 70 hipertansif hasta alındı. Bu hastaların 24 saat kan basıncı ölçümü holter ile değerlendirildi ve herbirinde 35 hasta olan iki gruba ayrıldı. Aort çapları M mod ve iki boyutlu ekokardiyografi ile değerlendirildi. Bu paramatreler iki gurup arasında karşılaştırıldı.

Bulgular: Dipper gurupta yaş ortalaması 55±11 yıl olan 26 kadın, 9 erkek hasta vardı. Non-dipper gurupta yaş ortalaması 56±11 yıl olan 25 kadın, 10 erkek hasta vardı. Temel özellikler açısından iki gurup arasında anlamlı farklılık yoktu. Non-dipper gurupta torasik aort çapları dipper guruba göre yüksekti (35.6±2.4 and 33.23±1.1, p<0.01).

Sonuç: Bu bulgular non-dipper hipertansiyon hastalarında torasik aort çaplarının yüksek olduğunu göstermiştir.

Anahtar Kelimeler: Kan basıncı, metabolik sendrom, aort çapı, ekokardiyografi, non-dipper

Introduction

Normal variation in blood pressure (BP) is characterized by a 10% to 20% reduction in BP from day to night [1]. Individuals with this decline in nocturnal BP are known as "dippers", and those who experience a blunted decline in nocturnal BP are known as "non-dippers" [2]. Several studies involving subjects with uncomplicated essential hypertension have revealed an association between the non-dipper BP profile and increased risk of target organ damage at the cardiac, vascular and cerebrovascular levels [3, 4].

Hypertensive patients with metabolic syndrome are at high risk for the development of cardiovascular disease. Previous research has shown that 24-h ambulatory blood pressure monitoring (ABPM) is a better predictor of subsequent complications than spot measurements of blood pressure [5, 6]. More recent study has shown that metabolic syndrome has a deleterious effect on aortic function [7]. Further, the effect of non-dipping BP on aortic root diameter in patients with metabolic syndrome has yet to be sufficiently investigated.

In this study, we investigated the association of non-dipping BP on aortic diameter in patients with metabolic syndrome.

Materials and Methods

Patients admitted to the cardiology department between August 2012 and December 2012, diagnosed as hypertensive

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and fulfilling the criteria for metabolic syndrome according to *National Cholesterol Education Program* (*NCEP*)- Adult Treatment Panel (NCEP/ATP-III) were eligible for the study. Patients were evaluated with 24-hour blood pressure Holter monitoring. Eligible patients were consecutively enrolled in the study until the dipper and non-dipper groups each reached 35 patients, for a total of 70 patients. Patients with thoracic aortic dilatation, diabetes mellitus, secondary hypertension, renal failure, hepatic failure, major cardiac disease (i.e., heart failure defined as left ventricular ejection fraction <50%, coronary artery disease, arrhythmias, cardiac valvular disease), and those receiving antihypertensive medication were excluded from the study. Thoracic aortic dilatation is defined as a measurement that exceeds normal range for a given age and body size. An aneurysm is defined as a 50% increase above this range [8].

The study was approved by the Institutional Ethics Committee, and written consent was obtained from all patients. During the baseline examination, fasting weight, height, waist circumference and hip circumference were measured by the same examiner using the ambulatory standard measurement devices while the patient was standing. Body mass index (BMI) was calculated using the formula "weight (kg)/height (m^2)." Clinical blood pressure measurements were performed using a mercury sphygmomanometer following 10 minutes rest in the sitting position. Three consecutive readings were taken with two minute intervals, and the mean of these readings was considered as clinical BP. The 24-hour ABPM was performed using a portable digital recorder (Bravo HR ABP, Sun Tech Medical Inc., Morrisville, NC, USA). The recorder was programmed to function between 07 AM-11 PM (diurnal BP values) for every 20 minutes and between 11 PM-07 AM for every 30 minutes (nocturnal BP values). Patients with a mean circadian systolic BP of >130 mmHg and/or diastolic BP of >80 mmHg were considered to be hypertensive [9].

The percent change in nocturnal blood pressure decline was calculated as**:**

Nocturnal BP decline (%)=(mean diurnal BP-mean nocturnal BP)x100/mean diurnal BP.

Biochemical Studies

Blood samples were collected from all patients after a fasting period of 12 h. Serum glucose, urea, creatinine, total cholesterol, triglycerides, HDL, and low-density lipoprotein cholesterol (LDL) levels were analyzed.

Echocardiographic Measurements

All echocardiograms were performed by the same investigator using the same device (Vivid Seven, GE Vingmed Ultrasound, Horten, Norway) with 3.5 MHz probe. The echocardiographic studies were performed in the left lateral decubitus position. Measurements and recordings were made during normal breathing at end-expiration. Diastolic ventricular septal thickness (IVSd), diastolic posterior wall thickness (PWd), left ventricular end-diastolic (LVEDD), left ventricular end-systolic dimensions (LVESD), and left ventricular ejection fraction (LVEF) (using the Teichholz method) were measured according to American Echocardiography Association recommendations [10]. Left ventricular mass and relative wall thickness (RWT) were estimated by left ventricular cavity dimension and wall thickness at end-diastole for all patients. For RWT, a value >0.45 was considered as normal for both genders. The sample volume of pulse wave Doppler was placed between the tips of the mitral leaflets on the apical 4-chamber view and from the transmitral flow tracing; peak velocity of early diastolic filling (E), late filling with atrial contraction (A), and E/A ratio were also obtained [11]. The mitral annulus peak early diastolic velocity (Em), late diastolic velocity (Am) and systolic velocity (Sm) were measured at the lateral corner of the mitral annulus by the same echocardiographic unit by activating tissue Doppler imaging mode in the apical 4-chamber view. The aortic diameters were measured with M-mode and two dimensional studies at the level of Valsalva sinus, sinotubuler junction and tubular aorta in the parasternal long-axis view.

The following formulas were used to calculate LV Mass [12] and RWT [13]:

$$\text{LV Mass (g)} = 0.8\{1.04[([\text{LVEDD}+\text{IVSd}+\text{PWd}]^3-\text{LVEDD}^3)]\}+0.6$$

$$\text{RWT} = 2\,(\text{PWd})/\text{LVEDD}$$

LVEDD: Left ventricular end diastolic diameter; IVSd: Diastolic ventricular septal thickness; PWd:Diastolic posterior wall thickness; RWT: relative wall thickness.

Statistical Analysis

Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) 13.0 for Windows (IBM, Illinois, USA). Continuous variables are presented as the mean±standard deviation, and categorical variables are presented as percentages. The between group differences for the categorical varieties were compared with the chi-square or Fisher's exact test. According to the distribution, the between group differences for the continuous variables were compared by either Student's t-test or the Mann-Whitney U test. The significance level was set at $p<0.05$.

Results

Patients were divided into two groups according to the percent decline in systolic and diastolic blood pressures; as either dipper (≥10%; n=35, 26 women, 9 men; mean age 55±11 years) or non-dipper (<10%; n=35, 25 women, 10 men; mean age 56±11 years). There were no significant differences

Table 1. Comparison of basal clinical features and holter parameters of study subjects

	Dipper (n:35)	Non-Dipper (n:35)	p value
Age (year)	55±11.13	56±11.05	NS
Gender (male/female)	9/26	10/25	NS
Height (cm)	167.2±8.1	165±7.7	NS
Weight (kg)	81.0±10.6	79.9±8.7	NS
Body mass index (kg/m^2)	29±3.4	29.4±3.5	NS
Waist circumference (cm)	96.2±11	97.6±9.9	NS
Systolic blood pressure (mmHg)	146.2±10.1	148.4±9.3	NS
Diastolic blood pressure (mmHg)	88.2±3.8	92.2±4.3	NS
Biochemical parameters			
Glucose (mg/dL)	103.3±17.27	103.6±15.76	NS
Urea (mg/dL)	18.2±4.5	17.6±3.8	NS
Creatinine (mg/dL)	0.7±0.2	0.7±0.4	NS
Triglyceride (mg/dL)	227.3±93.0	220.7±90.4	NS
Total cholesterol (mg/dL)	169.8±26.5	164.7±36.3	NS
HDL-cholesterol (mg/dL)	37.9±7.3	39.7±7.7	NS
LDL-cholesterol (mg/dL)	114.3±41.5	138.8±36.4	NS
Platelet count (x10^3/mm^3)	23.4±1.6	22.1±1.6	NS
RDW	14.3±1	13.9±1.2	NS
Blood pressure (holter) (mmHg)			
24 hours systolic	130.6±13	143.2±19.1	0.175
24 hours diastolic	79.5±9.5	83.5±11.1	0.46
Nighttime systolic	115.1±19.2	140.4±18.1	<0.001
Nighttime diastolic	68.6±9.5	80.9±10	<0.001
Daytime systolic	137.4±14	139.6±35.4	0.732
Daytime diastolic	84.7±10.3	84.9±12.3	0.985
Change of day and night mean pressures (%)			
Systolic pressure	12.6	4.3	0.001
Diastolic pressure	13.1	6.2	0.001

Data are expressed as the means±SD; NS: nonsignificant; HDL: high-density lipoprotein; LDL: low-density lipoprotein; RDW: red blood cell distribution width; BMI: body mass index;

between the two groups with respect to age, gender distribution, height, weight, body mass index, waist circumference or mean systolic and diastolic blood pressures (Table 1). The mean nocturnal measures of systolic and diastolic blood pressure were significantly higher in the non-dipper group (140.4±18.1 mmHg vs 115.1±19.2 mmHg and 80.9±10 mmHg vs 68.6±9.5 mmHg, respectively, p<0.001; Table 1).

Assessment of the distribution of metabolic syndrome components according to NCEP/ATPIII criteria in the dipper group revealed that 35 (100%) patients were hypertensive, 11 (31%) patients had high blood glucose, 31 (89%) patients had low a HDL level, 26 (77%) patients had hypertriglyceridemia, and 25 (71%) patients had increased waist circumference. In the non-dipper group, 35 (100%) patients were hypertensive,

Table 2. Comparison of conventional echocardiographic features of dipper and non-dipper patients

	Dipper (n:35)	Non-Dipper (n:35)	p value
LVEDD (mm)	46.1±0.3	46±0.7	NS
LVESD (mm)	30±0.3	31.3±0.8	NS
EF (%)	62±3.7	60.7±6.7	NS
MPI	0.55±0.8	0.59±0.4	NS
LVM (g)	179±48.5	197±40.8	NS
LV Mass Index (g/m^2)	95.4±25.3	101±28.6	NS
RWT	0.471±0.065	0.470±0.059	NS
E (cm/s)	0.6 ±0.1	0.7±0.3	NS
A (cm/s)	0,7±0.1	0.8±0.1	NS
E/A ratio	0.9±0.2	0.9±0.4	NS
Mitral Annulus			
Early diastolic velocity (Em)	0.08±0.03	0.12±0.18	NS
Late diastolic velocity (Am)	0.09±0.01	0.10±0.02	NS
LV (Sm)	0.11±0.03	0.12±0.01	NS
Em/Am	0.81±0.11	0.79±0.21	NS
Thoracic Aorta diameter (tubular level) (mm)	33.23±1.1	35.6±2.4	0.01
Thoracic Aorta diameter (tubular level) (mm/m^2)	14.8±0.56	17.2±1.15	0.01

LVEDD: left ventricular end diastolic diameter; LVESD: left ventricular end systolic diameter; EF: ejection fraction; MPI: myocardial performance index, LV (Sm); Left ventricular systolic myocardial velocity; LVM: left ventricular mass; RWT: relative wall thickness; Data are expressed as the means±SD; NS: nonsignificant

13 (37%) patients had high blood glucose, 29 (82%) patients had a low HDL level, 27 (80%) patients had hypertriglyceridemia, and 25 (71%) patients had increased waist circumference. According to the metabolic syndrome components ratio, there was no significant difference between the two groups (p=0.318).

When compared in terms of echocardiographic features, both groups were similar in left ventricular chamber diameters and standard Doppler parameters. There were no significant between group differences in conventional echocardiography parameters E, A, and E/A. Among tissue Doppler parameters Em, Am, Sm and Em/Am, the dipper and non-dipper groups were similar. When thoracic aorta measurements were analyzed, non-dipper patients had a significantly higher thoracic aortic diameter value than dipper patients (36.6±2.4 and 33.23±1.1, p<0.01; Table 2).

Discussion

Aging and hypertension have been shown to significantly increase aortic diameter. Aortic root dilatation is a frequent cardiovascular phenomenon in hypertensive patients who are referred to echocardiography laboratories for identification of hypertensive organ damage and is predictive of increased cardiovascular morbidity and mortality [14]. Aortic root dilatation is considered a useful marker of subclinical left ventricular diastolic dysfunction [15].

Endothelial dysfunction, inflammatory response (cytokines), and renin-angiotensin system activation are the common underlying pathophysiological mechanisms in metabolic syndrome [16]. These mechanisms lead to vascular tonus alterations and vascular hypertrophy. Hypertrophy and hyperplasia in smooth muscles with increased collagen synthesis causes increased arterial stiffness [17]. In hypertensive

individuals, the principal structural modification of the vessel wall is the hypertrophy of the medial layer [18, 19]. Medial hypertrophy is associated with considerable development of the extracellular matrix of the media and even the adventitia. These histopathologic changes result in reduced compliance, and distensibility of the arterial wall (20). Thus, the deterioration of aortic function may be an early predictor of coronary atherosclerosis and show end organ damage in hypertensive subjects. In such patients, the failure of blood pressure to normally decrease at night is called the non-dipper pattern and is associated with increased exposure to barotrauma. Physiologically, the nocturnal decline in blood pressure is a protective mechanism that decreases the pressure load of the arterial wall. Unlike patients who are dippers, patients with the non-dipper pattern of nocturnal blood pressure lack this protective response, and consequently the aortic wall is exposed to additional pressure load, which can result in prominent aortic function deterioration [21, 22].

The two study groups had similar echocardiographic evaluation results related to ventricular function. Myocardial performance index, which reflects global left ventricular function, was higher in non-dipper group, but this difference was not significant, and left ventricular systolic function was similar in both groups. These findings support the similarity in diastolic function between dippers and non-dippers [23].

Although our small sample size (n=70) is a study limitation, we were still able to show that aortic diameter is significantly higher in non-dipper hypertensive patients with metabolic syndrome than similar dipper patients. To the best of our knowledge, this study is the first to document aorta diameters in non-dipper hypertensive patients with metabolic syndrome. Current data suggest that hypertensive patients identified with ABPM as non-dippers require a more aggressive treatment approach. We believe that hypertension should be carefully monitored in patients with metabolic syndrome to identify those with the non-dipper BP pattern and that such patients should be carefully followed and promptly treated to minimize aortic dysfunction risk.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Bursa Yuksek Ihtisas Training and Research Hospital/ 2013-978.

Informed Consent: Written informed consent was obtained from all patients who participated in this study.

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