The influence of dipper and nondipper blood pressure patterns on left ventricular functions in hypertensive patients: a tissue Doppler study

Hipertansif hastalarda dipper ve non-dipper kan basıncının sol ventrikül fonksiyonları üzerine etkisi: Doku Doppler çalışması

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Objectives: We investigated the effect of dipper and non-dipper blood pressure patterns on left ventricular diastolic filling parameters in hypertensive patients.

Study design: Fifty-five hypertensive patients (37 women, 18 men; mean age 55±10 years) were evaluated with echocardiography and ambulatory 24-hour blood pressure monitoring. All the patients received antihypertensive drug therapy for at least three months prior to the evaluations. Tissue Doppler-derived systolic and diastolic parameters were compared.

Results: Dipper and nondipper blood pressure patterns were found in 22 patients (40%) and 33 patients (60%), respectively. Both groups had similar left ventricular systolic and diastolic diameters. Dipper patients had significantly lower values for left atrial diameter (p<0.0001), interventricular septum (p=0.001) and posterior wall (p=0.012) thickness, left ventricular mass (p=0.017) and mass index (p=0.021). Both groups had similar mitral E and A waves, E/A ratio, E-wave deceleration time, isovolumetric relaxation time, and tissue Doppler-derived A' wave. Dipper patients had a significantly lower E/E' ratio (10.8±3.4 *vs.* 14.1±3.6; p=0.002) and significantly higher systolic (S') (p=0.05) and early diastolic (E') (p=0.027) tissue velocities. Based on the E/E' ratios being <15 or ≥15, the frequency of dipper hypertension was significantly higher in patients with E/E' <15 (48.8% *vs.* 9.1%; p=0.019). The frequency of dippers was also higher among patients having an E/E' ratio of <8, compared to those having an E/E' ratio of ≥8 to <15 (90% *vs.* 35.3%; p=0.019).

Conclusion: Nondipper blood pressure pattern may be associated with increased left ventricular mass, impaired left ventricular systolic and diastolic dysfunction, and higher left ventricular filling pressures.

Key words: Blood pressure monitoring, ambulatory; circadian rhythm; echocardiography, Doppler; hypertension; ventricular dysfunction, left.

Amaç: Hipertansif hastalarda dipper ve non-dipper kan basıncı tiplerinin sol ventrikül diyastolik doluş parametreleri üzerindeki etkisi araştırıldı.

Çalışma planı: Hipertansif 55 hastada (37 kadın, 18 erkek; ort. yaş 55±10) ekokardiyografik inceleme ve 24 saatlik ambulatuvar kan basıncı izlemesi yapıldı. Değerlendirmelerden önce tüm hastalar en az üç ay süreli antihipertansif ilaç tedavisi görmekteydi. Doku Doppler ile elde edilen sistolik ve diyastolik parametreler karşılaştırıldı.

Bulgular: Yirmi iki hastada (%40) dipper, 33 hastada (%60) non-dipper kan basıncı saptandı. Sol ventrikül sistolik ve diyastolik çaplar iki grupta benzer bulundu. Dipper grubunda sol atriyum çapı (p<0.0001), interventriküler septum (p=0.001) ve posteriyor duvar (p=0.012) kalınlıkları, sol ventrikül kütlesi (p=0.017) ve kütle indeksi (p=0.021) anlamlı derecede düşük bulundu. İki grup arasında mitral E ve A dalgası, E/A oranı, E dalga yavaşlama zamanı, izovolümik gevşeme zamanı ve doku Doppler ile hesaplanan A' dalgası açısından farklılık yoktu. Dipperli hastalarda E/E' oranı (10.8±3.4 ve 14.1±3.6; p=0.002) daha düşük bulunurken, sistolik (S') (p=0.05) ve erken diyastolik (E') (p=0.027) doku hızları anlamlı derecede daha yüksek idi. E/E' oranı <15 ve ≥15 olarak gruplandırıldığında, E/E' <15 olan grupta dipperli hasta oranı anlamlı derecede yüksek idi (%48.8 ve %9.1; p=0.019). Benzer şekilde, E/E' <8 olan hastalar arasında dipperli oranı, E/E' ≥8 ve <15 olan hastalara göre belirgin derecede yüksek bulundu (%90 ve %35.3; p=0.019).

Sonuç: Hipertansif hastalarda non-dipper kan basıncının sol ventrikül kütlesinde artış, sol ventrikül sistolik ve diyastolik fonksiyonlarda bozulma ve sol ventrikül dolum basınçlarında artış ile ilişkili olduğu görülmektedir.

Anahtar sözcükler: Kan basıncı izlemesi, ambulatuvar; sirkadyen ritim; ekokardiyografi, Doppler; hipertansiyon; ventrikül disfonksiyonu, sol.

Received: December 2, 2008 *Accepted:* February 4, 2009

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Systolic and diastolic blood pressure decrease more than 10% during sleep compared to daytime. This diurnal pattern is considered to be normal. The term 'nondipper' refers to patients whose blood pressure do not demonstrate this diurnal pattern.[1] Nondipper patients have a higher cardiovascular risk and target organ damage than dippers.[2-7] Diastolic dysfunction is common among hypertensive individuals having left ventricular hypertrophy and increased intracardiac pressure.[8-12] Dipper and nondipper blood pressure patterns have been studied extensively among hypertensive patients. However, studies investigating the association of these patterns with left ventricular diastolic filling parameters reported conflicting results.[13-16] This study was designed to investigate the effect of these blood pressure patterns on left ventricular diastolic filling parameters.

PATIENTS AND METHODS

Fifty-five patients (37 women, 18 men; mean age 55±10 years) with a history of chronic hypertension and receiving appropriate antihypertensive medications were prospectively enrolled. The diagnosis of hypertension was based on the criteria proposed by the World Health Organization and International Society of Hypertension.[17] All the patients received the same drug therapy for at least three months prior to enrollment. Exclusion criteria included the presence of the following: known coronary artery disease, positive treadmill test or nuclear perfusion stress test, ischemic electrocardiographic findings, chronic renal failure, moderate or severe valvular stenosis or insufficiency, diabetes mellitus, congenital heart disease, left ventricular systolic dysfunction on echocardiography, anemia, hyperthyroidism, pregnancy, obstructive sleep apnea, and atrial fibrillation. Secondary causes of hypertension were investigated and patients with secondary hypertension were excluded. Patients who were treated with beta-blockers or nondihydropyridine calcium antagonists were not enrolled in the study. There was no washout period for the antihypertensive drug treatment. Written informed consent was obtained from all the patients. Following history taking and physical examination, each patient was assessed using 12-lead electrocardiography and transthoracic echocardiography.

Echocardiographic examination. Standard echocardiographic examination was performed using a Vingmed Vivid System 5 device (General Electric, Norway) with a 2.5-MHz transducer. Two-dimensional echocardiographic examination was performed from standard parasternal long- and short-axes and apical two-, three- and four-chamber views. Left ventricular (LV) systolic and diastolic diameters, and diameters of the left atrium (LA) and aorta, and LV ejection fraction (by the biplane Simpson's method) were measured by two-dimensional and classical M-mode echocardiography. Left ventricular mass and mass index were calculated by the recommended formulas in the literature.[18,19] Mitral inflow E and A waves, E-wave deceleration time, and isovolumetric relaxation time were obtained from the apical four-chamber view. Tissue Doppler imaging (TDI) was performed with a frequency of 2.5-3.5 MHz using second harmonic imaging from the apical two-, three, and four-chamber views. Images were recorded digitally (EchoPac 6.3, Vingmed General Electric). The sample volume was placed in the basal septal and lateral segments of the interventricular septum and systolic, diastolic E'- and A'-wave velocities were obtained. In order to determine the left ventricular global systolic and diastolic functions, basal septal and lateral systolic, early and late diastolic velocities were averaged (LV-TDI S', LV-TDI E' and LV-TDI A'). Simultaneous electrocardiographic recording was performed throughout TDI examination.

Ambulatory 24-hour blood pressure monitoring was performed following echocardiographic evaluation (GH Medical Inc, Model 88, Minneapolis, USA). Automatic blood pressure recordings were obtained regularly every 30 minutes during the 24-hour period. The cuff was placed around the nondominant arm of the subjects. The subjects were questioned about their sleep quality and 24-hour blood pressure assessments were repeated if necessary. Sleep and awake periods were assessed based on the information obtained from the patients. Nocturnal blood pressure dipping was calculated using the following formula: (%) 100 x [1 – (sleep systolic blood pressure/awake systolic blood pressure)]. Nocturnal blood pressure dipping was defined as more than 10% decrease in both nocturnal systolic and diastolic blood pressures compared to the average daytime blood pressures. Detection of less than 10% decrease in either systolic or diastolic blood pressures was regarded as nondipper hypertension.[20]

Statistical analysis. Statistical data were processed using the SPSS for Windows statistical package. Continuous variables were expressed as mean ± standard deviation (SD) and were compared between groups using the two-tailed Student's t-test. Nonparametric variables were analyzed using the Mann-Whitney U-test. Fisher's exact test (chi-square)

Table 1. Characteristics of dipper and nondipper hypertensive patients

	Dipper (n=22)			Nondipper (n=33)			
	n	%	Mean±SD	n	%	Mean±SD	*p*
Age (years)			53±11			57±10	NS
Sex							NS
Males	7	31.8		11	33.3		
Female	15	68.2		22	66.7		
Smoking	9	40.9		13	39.4		NS
Body mass index (kg/m^2)			29.0±1.8			28.0±2.1	NS
Medications							
ACE inhibitors	8	36.4		13	39.4		NS
Calcium channel blockers	6	27.3		8	24.2		NS
Angiotensin receptor blockers	8	36.4		12	36.4		NS
Diuretics	16	72.7		25	75.8		NS
Combined regimen	14	63.6		24	72.7		NS
Systolic blood pressure (mmHg)			123±12			131±13	NS
Diastolic blood pressure (mmHg)			78±8			80±12	NS
Total cholesterol (mg/dl)			198±34			204±43	NS
LDL-cholesterol (mg/dl)			128±23			133±28	NS
HDL-cholesterol (mg/dl)			36±12			38±18	NS
Triglyceride (mg/dl)			176±34			188±33	NS
Fasting glucose (mg/dl)			92±12			96±10	NS
Creatinine (mg/dl)			0.9±0.1			0.9±0.2	NS

NS: Not significant.

was used for comparison of categorical variables. A *P* value of less than 0.05 was accepted as significant.

RESULTS

According to the 24-hour ambulatory blood pressure monitoring, dipper and nondipper hypertension were found in 22 patients (40%) and 33 patients (60%), respectively. Clinical and demographic characteristics of the patients are demonstrated in Table 1 and echocardiographic findings are summarized in Table 2. Both groups were similar in terms of age, systolic and diastolic blood pressures, and antihypertensive drugs used.

Dipper and nondipper patients had similar left ventricular systolic and diastolic diameters. Thirty-seven patients were found to have impaired relaxation and 17 patients had a pseudonormal left ventricular diastolic filling pattern. There were no patients with a restrictive filling pattern. The ratios of impaired relaxation and pseudonormal filling patterns were also similar between dipper and nondipper patients. However, dipper patients had significantly lower values for LA diameter (p<0.0001), interventricular septum (p=0.001) and posterior wall (p=0.012) thickness, left ventricular mass (p=0.017), and mass index (p=0.021). Both groups were similar in terms of mitral E and A waves, E/A ratio, E-wave deceleration time, isovolumetric relaxation time, and TDI-derived A' wave. Dipper patients had significantly lower E/E' values (10.8±3.4 *vs*. 14.1±3.6; p=0.002) and significantly higher systolic (S') (6.7±1.1 cm/sec *vs*. 6.3±0.7 cm/sec; p=0.05) and early diastolic (E') (-6.7±2 cm/sec *vs*. -5.6±1.7 cm/sec; p=0.027) tissue velocities (Table 2).

The patients were further evaluated in two subgroups based on the E/E' ratios being E/E' ≥15 (n=11) or E/E' <15 (n=44), with the mean E/E' ratios being 18.2±3.2 and 11.4±2.6, respectively (p<0.0001). Patients with E/E' ≥15 had increased interventricular septum thickness (1.4±0.2 cm *vs*. 1.2±0.3 cm; p=0.03) and isovolumetric relaxation time (128±28 msec *vs*. 114±20 msec; p=0.05) and had significantly lower left ventricular tissue Doppler early diastolic (E') (-4.2±1.1 cm/sec *vs*. -6.5±1.8 cm/sec; p<0.0001) and systolic (S') (5.9±0.7 cm/sec *vs*. 6.6±0.9 cm/sec; p=0.02) velocities. There was also a significant difference between these two groups with respect to the frequency of dipper *vs*. nondipper hypertension (p=0.019). Of 44 patients having an E/E' <15, 21 patients (47.7%) were dippers, whereas only one patient (9.1%) had dipper hypertension among 11 patients with an E/E' ≥15. Other echocardiographic parameters were similar between the two groups.

Patients having an E/E' ratio below 15 were also evaluated based on a cutoff value of 8 for E/E'. The mean E/E' ratios were 12.6±1.5 and 7.4±0.5 in subgroups of E/E' <8 (n=10) and E/E' ≥8 (n=34) (p

Table 2. Echocardiographic findings of dipper and nondipper hypertensive patients

	Dipper (n=22)			Nondipper (n=33)			
	n	%	Mean±SD	n	%	Mean±SD	*p*
Left atrium diameter (cm)			3.3±0.3			4.0±0.6	<0.0001
Aortic diameter (cm)			3.0±0.4			3.3±0.5	N S
Left ventricular diastolic diameter (cm)			4.8±0.5			4.9±0.7	N S
Left ventricular systolic diameter (cm)			3.0±0.5			2.9±0.5	N S
Interventricular septum thickness (cm)			1.1±0.2			1.3±0.2	0.001
Posterior wall thickness (cm)			1.0±0.2			1.1±0.2	0.012
Left ventricular mass (g)			188±54			279±116	0.017
Left ventricular mass index (g/m^2)			112±32			157±57	0.021
Left ventricular diastolic filling pattern							N S
Impaired relaxation	17	77.3		20	60.6		
Pseudonormal	5	22.7		13	39.4		
Mitral E maximal velocity (E) (m/sec)			0.68±0.13			0.73±0.11	N S
Mitral A maximal velocity (A) (m/sec)			0.8±0.2			0.8±0.2	N S
E/A			0.88±0.29			0.93±0.27	N S
E-wave deceleration time (msec)			202±56			194±42	N S
Isovolumetric relaxation time (msec)			112±22			119±22	N S
Tissue doppler							
Left ventricular systolic velocity (S') (cm/sec)			6.7±1.1			6.3±0.7	0.05
Left ventricular early diastolic velocity (E') (cm/sec)			-6.7±2.0			-5.6±1.7	0.027
Left ventricular late diastolic velocity (A') (cm/sec)			-7.9±1.5			-8.2±2.3	N S
E/E'			10.8±3.4			14.1±3.6	0.002
E/E' >15	1	4.6		10	30.3		0.019
E/E' <15	21	95.5		23	69.7		

NS: Not significant.

<0.0001). Those having an E/E' of ≥8 exhibited a female preponderance (26 of 34 *vs*. 3 of 10; p=0.006), older age (56±11 years *vs*. 48±10 years; p=0.05), increased LA diameter (3.8±0.6 cm *vs*. 3.3±0.3 cm; p=0.017) and E-wave deceleration time (225±54 msec *vs*. 187±46 msec; p=0.03), and significantly decreased left ventricular tissue Doppler systolic (S') (6.3±0.7 cm/sec *vs*. 7.4±0.9 cm/sec; p=0.001) and early diastolic (E') (-5.8±1.1 cm/sec *vs*. -8.8±1.8 cm/sec; p<0.0001) velocities. The frequency of nondipper patients was also higher in this group (22 of 34 *vs*. 1 of 10; p=0.019).

DISCUSSION

Left ventricular diastolic dysfunction may develop before left ventricular hypertrophy and systolic dysfunction in hypertensive patients.[8-10] Up to 50% of patients who present with heart failure symptoms have preserved left ventricular systolic functions.[11,12] Tissue Doppler-derived myocardial wall motion parameters have been found to be less preload-dependent compared to the transmitral flow patterns and more specific in the diagnosis of diastolic dysfunction.[21-23] The E/E' ratio is a new and reliable parameter that represents left ventricular filling pressures.[24] Tissue Doppler-derived systolic wall motion velocity parameters are relatively load-independent and sensitive indices for the early diagnosis of left ventricular systolic dysfunction compared to the conventional echocardiographic parameters.[25] Patients with nondipper blood pressure characteristics have higher cardiovascular complications and target organ damage.[1,3,26,27] Early detection of left ventricular systolic and diastolic dysfunction and its association with end-organ damage and the utility of ambulatory blood pressure monitoring may need further investigation as there are conflicting results regarding this topic.[13-16]

We aimed to investigate the subclinical systolic and diastolic dysfunction among dipper and nondipper hypertensive patients who had been treated with appropriate antihypertensive drugs. We used TDI-derived systolic and diastolic velocities for this purpose. Although there were no differences between dipper and nondipper patients in terms of conventional echocardiography-derived systolic and diastolic parameters, the E/E' ratio was significantly higher in nondippers. Despite the higher frequency of the pseudonormal filling pattern in the nondipper group, this difference was not statistically significant. Increased E/E' ratio in nondipper patients represents increased left ventricular filling pressures, which may be a predictor of impending diastolic dysfunction.

Almost all the patients with an E/E' ratio below 8 were dippers, suggesting normal ventricular filling pressures in this group. Nondipper patients also had significantly greater LA diameter, interventricular septum and posterior wall thickness, and left ventricular mass. These findings may be interpreted as increased intracavitary pressure among this group. Tissue Doppler-derived left ventricular systolic velocities were lower in nondippers, suggesting subclinical systolic dysfunction in this group. Further studies are required to determine the need for a more aggressive antihypertensive treatment to improve cardiovascular prognosis in nondipper hypertensive patients. Our results are consistent with those of Seo et al.[15] We hypothesized that nondipper patients would benefit from a more aggressive antihypertensive regimen with target blood pressure levels lower than general recommendations. Thus, detection and follow-up of nondipper and dipper hypertensive subjects with ambulatory blood pressure monitoring may be a useful strategy to identify individuals having a high prognostic risk.

Study limitations. Small sample size limits generalization of our findings. The study patients were on antihypertensive medications during the echocardiographic assessment and there was no drug washout period. This might have altered diastolic parameters.

In conclusion, nondipper nocturnal blood pressure pattern may be associated with increased left ventricular mass, impaired left ventricular systolic and diastolic dysfunction, and higher left ventricular filling pressure. Ambulatory blood pressure monitoring is a useful method to identify high-risk patients who may benefit from more aggressive strategies.

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