

Research Article

Evaluation of Left Ventricular and Left Atrial Functions with Strain and Strain Rate Echocardiography in Patients with Nondipper and Dipper Hypertension

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Abstract

Objectives: Nondippers hypertension (NDHT) are known to carry a high risk of cardiovascular morbidity and mortality. The aim of this study was to investigate the effects of dipper (DHT) and nondipper status of hypertension on left atrial (LA), left ventricle (LV) systolic and diastolic functions using two-dimensional echocardiography (2D), tissue Doppler images (TDI) and strain imaging.

Methods: A total of 60 patients and 20 healthy individuals were included in the study. The patients were separated two groups that dipper and nondippers (if their daytime ambulatory systolic and diastolic blood pressure did not decrease by at least 10% during the night). Left ventricle and LA strain values, diastolic function were obtained by 2D with automated software and compared between the groups.

Results: Demographic variables of the groups were similar in our study.(such as age, gender, smoker, body mass index, lipid profile) Diastolic functions significantly impaired in NDHT group (E velocity and E/A ratio were significantly reduced, A velocity a significantly increased, $p < 0.005$). Tissue Doppler measurements; Lateral S_m , E_m , Septal E_m were significantly reduced in NDHT group ($p < 0.005$). Strain parameters of patients was seen to be significantly reduced in NDHT group (LV lateral S, LV septal S, LA lateral S, LA septal S, $p < 0,005$).

Conclusion: Patients with nondipper hypertension have decreased LV diastolic function, significantly changes of tissue Doppler and analysis of left ventricle and atrial strain, in comparison with dipper group. In our study, both atrial and ventricular strain evaluations were found to be significantly impaired in the NDHT group at the same time. Consequently LV-LA strain can be used for the assessment early knowledge of the target organ damage in patients with nondipper hypertension.

Keywords: Hypertension, left atrial function, left ventricular function, tissue Doppler echocardiography, strain, strain rate

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Cardiovascular diseases lead major health problems in the world, and hypertension (HT) is a major risk factor for cardiovascular diseases and additionally stroke caused by hypertension leads to greater morbidity and mortality in hypertensive patients.^[1] Systolic and diastolic blood pressures 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 does not demonstrate this diurnal pattern.^[2] Nondipper hypertension (NDHT) is associated with increased cardiovascular morbidity and mortality, including atrial fibrillation, stroke, myocardial infarction and sudden cardiac death.^[3]

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Cardiovascular mortality, morbidity and cerebrovascular events increase in patients with NDHT, and left ventricular hypertrophy, impaired left ventricular (LV) systolic and diastolic function is more common in these patients. Two-dimensional (2D) pulse and tissue Doppler echocardiography are used to evaluate left atrial (LA) function and left ventricle (LV) systolic and diastolic function.^[4] Strain and strain rate echocardiography is a noninvasive method that provides valuable clinical information about the regional functions of both ventricles and atrial myocardium.^[5]

As a result, in this study, the effects of DHT and NDHT on LA and LV functions were compared with normal population using conventional echocardiography parameters, tissue Doppler, longitudinal strain and strain rate methods.

Methods

Study Groups

The hypertensive patients, referred to the Cardiology department between April 2017 and November 2018 and who had no target organ damage and met the study inclusion and exclusion criteria, were enrolled. The study was approved by the Ethics Committee of the Afyon Health Science University Hospital, and all individuals signed an informed consent form. Patients were placed into four groups.

The definition of hypertension was considered as systolic BP ≥ 140 mm Hg and/or diastolic BP ≥ 90 mm Hg, previously diagnosed hypertension, or use of antihypertensive drugs. All patients underwent ambulatory blood pressure monitoring (ABPM). Based on the ABPM results, patients were divided into DHT and NDHT groups. The control group was defined as no history of HT and no taking any antihypertensive drug.

The study included participants older than 18 years and younger than 80 years. Patients with any of the following were excluded from the study: coronary artery disease, type 1 or 2 (requiring insulin therapy) diabetes mellitus (DM), chronic obstructive pulmonary disease or obstructive sleep apnea syndrome, hepatorenal dysfunction, thyroid dysfunction, amyloidosis, cardiomyopathy with a left ventricular ejection fraction (LVEF) $< 50\%$, branch block, atrioventricular communication disorder, pericarditis, myocarditis, recent electrical cardioversion, malignancy, age outside the specified range, active infection, antiarrhythmic, antidepressant or antipsychotic, change of anti-HT therapy in last six months or antihistaminic drug usage.

Ambulatory Blood Pressure Monitoring

All patients included in this study underwent 24-h ABPM (Delmar Reynolds Medical Pressurometer[®], USA). The non dominant arm of patients was selected for the cuff placement. Then, 24-hour ABPM recordings were taken (blood

pressure was measured every 30 minutes during the day and every 60 minutes during the night). Being awake and sleep periods were assessed according to the information taken from the patients. Nocturnal BP dipping was calculated as: $(\%) 100 \times [1 - (\text{sleep systolic BP} / \text{awake systolic BP})]$. Dipper hypertension was regarded as a more than 10% decrease in systolic and diastolic BPs. Non-dipper hypertension was regarded as a less than 10% decrease in systolic and diastolic BPs.^[5]

Echocardiography

Echocardiography was performed with the Phillips HD 11 XE (Germany, 2008) with a 3.5 MHz transducer probe. A one-lead ECG was recorded continuously during the echocardiographic examination. The thicknesses of the posterior wall and interventricular septum, LA dimensions, LV end-systolic and end-diastolic diameters were obtained using M-mode in parasternal long axis. LVEF was calculated using Simpson's biplane method. The velocities of the mitral E wave and A wave, deceleration time of E wave and E / A ratio were acquired using pulsed Doppler from the apical four-chamber view on the mitral valve.

Furthermore, velocities and systolic times of the mitral lateral, mitral septal, annular basal segments were acquired using pulsed Doppler and tissue Doppler echocardiography from the apical four-chamber view. Tissue Doppler images (TDI) measurements were limited to 2 points in the patient and control groups, as factors that could lead to segmental wall motion disorders were eliminated as much as possible.

We recorded 2D grayscale harmonic images from apical four chamber views focused on the LA and LV longitudinal strain-strain rate to analyse the 2D moving images. All images were obtained at a frame rate of 160–210 frames/sn and saved in digital format for four consecutive cardiac cycles. The offline image analysis was performed with Strain Quantification software (Phillips Co. USA). All echocardiographic procedures were performed by the same operator. Measurements were made in accordance with the recommendations of the American Echocardiography Association.^[6] We showed that longitudinal strain and strain rate measurement from an apical four-chamber image in Figure 1.

Statistical Analysis

The SPSS for Windows software package (ver. 22; SPSS Inc., Chicago, IL, USA) was used for the statistical analysis. Qualitative variables were evaluated among the groups and Chi-square test was used. In the evaluation of the quantitative variables, the Independent Samples T test was used for the comparison of 3 independent groups in the comparison of One Way Anova Test and 2 independent groups. The results were evaluated at a confidence interval of 95% and significance level at $p < 0.05$ significance level.

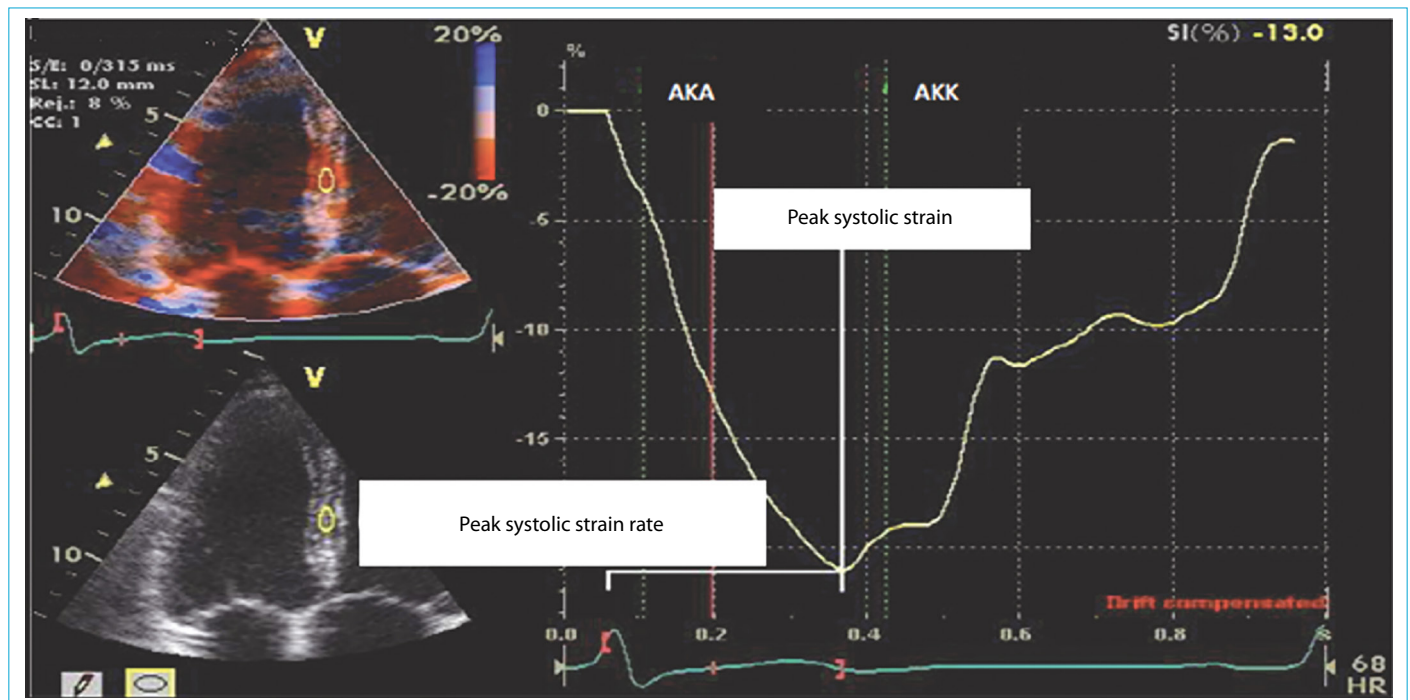


Figure 1. Longitudinal strain and strain rate measurement from an apical four-chamber image AKA: Aortic valve opening; AKK: Aortic valve closure.

Results

Baseline Characteristics and Ambulatory Blood Pressure Monitoring

Totally 60 patient included in the study. DHT and NDHT groups consisted of 30 patients and distribution of patients by gender was the same in both groups [12 of 30 patients male, 18 of 30 patient's woman]. Table 1 summarizes the clinical characteristics of the subjects. No statistical difference was observed between the groups in terms of general characteristics such as gender, age, smoking, weight, height, body mass index and lipid profile. Patient and control groups ABPM findings are presented in Table 1.

Echocardiography Findings

Septal thickness and posterior wall thickness values were significantly higher in NDHT patients compared to the DHT and control groups ($p=0.003$, $p=0.016$, respectively) (Table 2). While mean diastolic mitral flow velocity (E) was not different between DHT and NDHT groups, it was significantly higher in the control group ($p=0.004$).

The mean values of late diastolic mitral flow rate (A) between DHT, NDHT and control groups were significantly different (82.87 ± 17.44 , 96.57 ± 23.03 , 76.45 ± 18.85 , $p=0.002$, respectively). E/A mean values (0.97 ± 0.31 , 0.78 ± 0.25 , 1.19 ± 0.31 , $p=0.001$, respectively) showed a significant difference between the three groups (Table 2).

There were significant changes in tissue Doppler measurements and LV-LA M-Mode measurements between the groups. In particular, both LV and LA parameters were significantly impaired in the NDHT group (Table 2).

Discussion

Hypertension is a major and correctable cardiovascular risk factor. The correct diagnosis of hypertension and precise assessment of cardiovascular risk are essential to give proper treatment in patients with hypertension. Although echocardiography is the second-line study in the evaluation of hypertensive patients, it gives many clues suggesting bad prognosis associated with hypertension, including increased LV mass, decreased LV systolic function, impaired LV diastolic function, and increased LA size and decreased function.^[7,8]

In several studies comparing DHT and NDHT patients, strain analysis was observed in the NDHT group with speckle tracking method.^[4,9,10] However, in this patient group, we could not find any study evaluating both LV and LA functions with TDI longitudinal strain echocardiography method. In this study, we aimed to determine the relationship between longitudinal strain echocardiograph both LV and LA functions between DHT and NDHT groups.

Our found that LV mechanical functions, such as LV diastolic function, LV wall thickness, LV strain values and LA strain values, were significantly impaired in NDHT patients

Table 1. Baseline demographic and clinical characteristics of dipper and nondipper hypertensive patients and control groups

Variables	Dipper (n=30)	Nondipper (n=30)	Control (n=30)	p
Male (%)	12 (36.4)	12 (36.4)	9 (27.3)	0.926*
Women (%)	18 (38.3)	18 (38.3)	11 (23.4)	
Smoking (%)	8 (36.4)	8 (36.4)	6 (27.2)	0.959*
Age (years)	51.10±11.58	53.10±11.94	47.35±12.86	0.259**
Weight (kg)	79.60±10.51	77.17±9.67	75.85±9.18	0.392**
Length (cm)	165.27±8.47	161.5±6.10	165.35±6.79	0.082**
Waist Circumference (cm)	97.53±9.90	98.40±11.31	92.3±11.41	0.129**
BMI (kg/m ²)	29.12±3.10	29.62±3.70	28.02±3.20	0.259**
HT duration	3.07±4.11	4.47±4.51	–	0.214***
24-h SBP (mmHg)	140.16±10.04	141.66±13.85	–	0.63***
24-h DBP (mmHg)	86.00±6.48	85.00±7.98	–	0.59***
Dipper rate SBP/DBP (%)	16.8/12.3±5.21	6.4/7.1±3.21	–	0.001*
Total Kolesterol (mg/dl)	204.27±33.55	197.57±30.21	183.35±48.47	0.147**
Trigliserid (mg/dl)	157.8±72.73	135.17±58.03	130.10±47.02	0.221**
HDL kolesterol (mg/dl)	50.07±15.33	53.93±23.4	42±10.8	0.076**
LDL kolesterol (mg/dl)	131.4±27.71	121.37±33.88	114.05±37.76	0.178**
ACE/ARB, n (%)	14 (45.2)	17 (54.8)	–	0.001*
CCB, n (%)	5 (45.5)	6 (54.5)	–	0.111*
Diüretics, n (%)	8 (44.4)	10 (55.6)	–	0.017*
BB, n (%)	4 (44.4)	5 (55.6)	–	0.170*
ACE/ARB+CCB, n (%)	2 (50)	2 (50)	–	0.496*
ACE/ARB+Diüretics, n (%)	3 (37.5)	5 (62.5)	–	0.157*
ACE/ARB+BB, n (%)	1 (33.3)	2 (66.7)	–	0.472*
ACE/ARB+BB+Diüretics, n (%)	2 (50)	2 (50)	–	0.496*
ACE/ARB+CCB+Diüretics, n (%)	1 (25)	3 (75)	–	0.246*
All drug group, n (%)	1(100)	0	–	0.430*

*Ki-kare Test **One Way Anova Test *** Independent Samples T test # p<0.05 statistical significance, SBP: Systolic blood pressure; DBP:Diastolic blood pressure; HDL:High density lipoprotein; LDL:Low density lipoprotein; n: number; DHT: Dipper Hypertension; NDHT: Nondipper hypertension; BMI: Body mass index; ACE-ARB: Angiotensin converting enzyme inhibitor/ angiotensin receptor blocker; CCB: Calcium channel blocker; BB: Beta blocker.

compared with DHT and control groups. We did our work with TDI strain echocardiography.

There are different approaches for measuring myocardial strain by echocardiography. Strain data can be derived from either color-coded TDI or with speckle tracking echocardiography (STE) from B-mode grayscale images. The main advantage of STE is that it is reproducible, fast, and easy to use; on the other hand major drawbacks are a comparatively low frame rate of 2D grayscale images as well as anatomical and functional assumptions and the excessive smoothing. Because TDI-based strain allows much higher frame rates, it has far better temporal resolution, which is especially important for SR as its peaks are greatly influenced by short-lived events. Conventional TDI analysis, however, requires manual tracking of the myocardium through the cardiac cycle and so is cumbersome and time-consuming, with poor reproducibility.^[9] Also; although 2D-strain does not have the same

angle limitations as the Doppler-derived indices there is evidence that motion perpendicular to the ultrasound beam is prone to a higher degree of error.^[10]

The study by Modesto et al. involved 17 patients with amyloid cardiomyopathy and 10 normal controls. They measured the values obtained from the infero-septum and lateral walls at base, mid-cavity and apex using both techniques. They reported excellent correlation between STE-strain and TDI-strain for both strain and strain rate ($r=0.96$, $r=0.94$ respectively). It is important to note that they performed this technique over a wide range of left ventricular function and found that data was of a sufficient standard to be analysed in 92% of segments.^[11]

As a compensatory mechanism in the human body, the night pressure of blood pressure decreases the pressure load of the heart. As patients with NDHT were deprived of this procedure overnight, LV hypertrophy (LVH) and im-

Table 2. Echocardiographic results of patients and control groups

Variables	Dipper (n=30)	Nondipper (n=30)	Control (n=30)	p
LVEDD (mm)	48±4.41	47.97±4.23	46.95±3.23	0.620**
LVESD (mm)	31.03±3.31	31.27±4.04	30.6±4.04	0.830**
LVEF Simpson (%)	64.67±5.12	63.7±5.51	61.4±5.69	0.116**
IVS (mm)	11.5±1.65	10.8±1.66	9.95±0.99	0.003**
PW (mm)	11.23±1.56	10.8±1.44	10.05±0.94	0.016**
LA volume (ml/m ²)	39.6±7.27	38.9±10.71	34.9±5.13	0.130**
Mitral E (m/s)	77.33±17.23	71.46±14.21	88.10±18.81	0.004**
Mitral A (m/s)	82.87±17.44	96.57±23.03	76.45±18.85	0.002**
Mitral E/A	0.97±0.31	0.78±0.25	1.19±0.31	0.001**
Deceleration time (msn)	230.37±46.17	227.7±43.16	202.2±39.8	0.063**
Mitral E/Em	8.81±2.27	9.51±2.20	7.96±2.07	0.054**
LATSm (cm/s)	11.43±2.10	10.11±1.54	11.25±1.99	0.019**
LATEm (cm/s)	11.48±3.12	11.24±3.00	14.66±2.82	0.001**
LATAm (cm/s)	13.57±3.08	13.83±2.86	12.18±2.02	0.104**
SEPSm (cm/s)	9.81±1.42	9.25±1.54	9.59±0.88	0.281**
SEPEm (cm/s)	9.16±2.10	7.87±1.94	11.32±1.90	0.001**
SEPA m (cm/s)	12.93±2.48	12.42±2.32	11.4±1.88	0.072**
LV LAT Strain (%)	-20.51±0.73	-19.75±0.74	-24.15±1.21	0.001**
LV LAT Strain rate (1/sn)	-1.58±0.046	-1.42±0.55	-1.65±0.06	0.057**
LV SEP Strain (%)	-20.31±0.72	-19.68±0.65	-23.83±1.38	0.001**
LV SEP Strain rate (1/sn)	-1.54±0.04	-1.50±0.05	-1.62±0.15	0.001**
LA LAT Strain (%)	44.84±1.18	43.54±1.05	46.12±1.54	0.001**
LA LAT Strain rate (1/sn)	3.34±0.08	3.12±0.07	3.61±0.12	0.001**
LA SEP Strain (%)	44.64±1.33	43.46±1.08	45.53±1.57	0.001**
LA SEP Strain rate (1/sn)	3.30±0.07	3.11±0.09	3.56±0.12	0.001**

**One Way Anova Test. # p<0.05 significantly, n: Number; LVEDD: Left ventricular end diastolic diameter; LVESD: Left ventricular end systolic diameter; LVEF: Left ventricular ejection fraction; IVS: Interventricular septum; PW: Posterior Wall; LA: Left atrium; E: Early diastolic mitral flow velocities; A: Late diastolic mitral flow velocities; Em: Tissue Doppler early diastolic mitral annular velocities; LATSm: Lateral systolic mitral annular velocities; LATEm: Lateral early diastolic mitral annular velocities; LATAm: Lateral late diastolic mitral annular velocities; SEPSm: Septal systolic mitral annular velocities; SEPEm: Septal early diastolic mitral annular velocities; SEPA m: Septal late diastolic mitral annular velocities; LV: Left ventricle; LAT: Lateral; SEP: Septal.

paired LV diastolic stuffing were more common in these patients because LV was exposed to a longer pressure load.^[12] As a result, HT is an important cause of LV diastolic dysfunction and reduced LV compliance. Due to the increased LV stiffness and impaired blood flow from the left atrium to the left ventricle, the left atrium enlarges. In our study, septum and posterior wall thicknesses were found to be significantly higher in NDHT group as expected. In the DHT and NDHT studies of Ferrara et al.,^[13] E wave velocity and E/A ratio decreased in both groups, and A wave velocity increased significantly in NDHT group only. In our study, the differences between these three groups were found to be statistically significant, and E wave velocity and E/A ratio were decreased and A wave velocity increased with diastolic dysfunction.

Mitral annular velocity was decreased in hypertensive patients with normal ejection fraction. This may be used to

detect subclinical LV systolic dysfunction.^[14,15] In our study, mitral annular velocity (both lateral and septal) was significantly lower in the NDHT group. We believe that this reduction is important for detecting subclinical LV dysfunction and guiding treatment in patients with NDT.

ABPM is widely used for the evaluation of diurnal fluctuation of blood pressure. It has been demonstrated that ABPM is a better predictor of cardiovascular complications than the conventional, spot measurement of blood pressure. ABPM has become increasingly important for the management of hypertensive patients.^[16] In NDHT patients; cardiovascular events are poor prognostic factors in terms of LV function and arrhythmia development.^[17,18] The early detection of subclinical organ damage is very important in terms of treatment and prognosis in hypertension patients. In our study, we showed that there was a significant deterioration in both LV and LA longitudinal strains in NDHT pa-

tients using TDI echocardiography method. We think that this method should be used more widely in daily practice.

Seo and et al.,^[19] he had normal LV systolic functions and diastolic dysfunction in the NDHT patients. The E/Em ratio predicting LV filling pressure and diastolic dysfunction was also increased in the NDHT group. The authors also showed that systolic deformation and deformation rate decreased in their study. Similar results were observed with in our study. In our study, atrial strain parameters were found to be impaired in the NDHT group. The LV and LA strain and strain rate values were significantly impaired in DHT and NDHT groups compared to the control group. We think that this impairment may be associated with both functional and arrhythmic events of myocardium which may develop in HT patients.

Nowadays, HT is considered as the most common, independent and controllable risk factor for atrial fibrillation, and the risk of AF development in HT shows a moderate increase. It is understood that HT is the most frequent cause for AF when it is considered that it affects about 25–50% of the population in societies. HT is associated with left atrial dilatation and decreased left atrial conduction velocity. These changes in heart structure and physiology result in AF and ultimately thromboembolic complications. Applying aggressive antihypertensive treatment may improve cardiac structural changes in this group of patients and prevent or delay AF development.^[20]

In conclusion, we think that strain imaging technique can provide us to reach the early findings of target organ damage in the subclinical period in HT patients and may be a guide in follow-up and treatment.

Limitations of the Study

The main limitation of our study was the low number of patients participating in the study. In addition, the absence of a feasibility to compare two separate methods (speckle tracking-TDI strain echocardiography) at the same time was another important problem. The effects of antihypertensive agents on LA and LV mechanical functions in the patient groups was completely unknown and this state might have concealed the actual LA function.

Disclosures

Ethics Committee Approval: The ethics committee of Afyonkarahisar University of Health Sciences Clinical Research provided the ethics committee approval for this study (11.02.2019-2019/57).

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Authorship Contributions: Concept – E.B., Z.Y., A.A.; Design – E.B., A.A.; Supervision – A.A.; Materials – E.B., Z.Y.; Data collection

&/or processing – E.B., Z.Y.; Analysis and/or interpretation – E.B.; Literature search – E.B., Z.Y., A.A.; Writing – Z.Y., A.A.; Critical review – Z.Y., A.A.

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