

The relationship between osteoporosis and non-dipper hypertension in postmenopausal women

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ABSTRACT

Aims: Previous studies have shown association between hypertension and osteoporosis, however has not been evaluated alterations of circadian blood pressure patterns. The present study investigated the effects of osteoporosis on the circadian blood pressure assessed by ambulatory blood pressure monitoring.

Methods: 68 patients (mean age: 61.3±8.7 years, 34 dipper and 34 non-dipper patients) with postmenopausal hypertension (HT) were prospectively enrolled in this study. Ambulatory blood pressure monitoring was performed on all patients. We measured bone mineral density (BMD) and T-score by dual X-ray absorptiometry at the lumbar spine. The receiver operating characteristics (ROC) curve was used to demonstrate the sensitivity and specificity of lumbar spine BMD, optimal cut-off value for predicting non-dipper hypertension (NDHT).

Results: T-score and BMD in non-dipper patients were lower than the dipper patients. There was a significant correlation between the rate of fall in night of mean blood pressure and both lumbar spine T-score and lumbar spine BMD ($r=0.330$ and $P=0.006$ vs $r=0.322$ and $P=0.007$, respectively). A lumbar spine BMD <0.944 g/cm² measured by DXA had a 64.7% sensitivity and 64.7% specificity in predicting non-dipper hypertension at ROC curve analysis.

Conclusion: Low lumbar spine BMD is an independent and strong predictor of non-dipper hypertension. Osteoporosis may be an indicator of cardiovascular risk. Therefore, osteoporotic patients should be treated more aggressively.

Keywords: Menopause, non-dipper hypertension, osteoporosis

INTRODUCTION

Hypertension (HT) is a common disorder throughout society and it represents an important risk factor for cardiovascular diseases.¹ It is known that the blood pressure measured by ambulatory blood pressure monitoring (ABPM) predicts the cardiovascular event risk better than blood pressure measured in office.² As is already known, blood pressure has a circadian rhythm and this rhythm can be non-invasively assessed by ABPM. Among patients with essential HT, almost 25% also have non-dipper hypertension (NDHT).³ The pathophysiological mechanism underlying NDHT is not yet fully understood. It is known that the rate of target organ damage among patients with NDHT is higher than the rate in patients with dipper hypertension (DHT).⁴

Osteoporosis is one of the causes of morbidity and mortality in the elderly. In women, the incidence of both osteoporosis and HT increases with menopause. HT was

shown to be more common among osteoporotic women than non-osteoporotic women. This was explained by the elevation in the incidence of arterial stiffness and the levels of osteoprotegerin that occur concomitant to osteoporosis.⁵ Interestingly, previous studies have demonstrated increased osteoporosis incidence in hypertensive patients and some even argued that HT is a risk factor for fractures.⁶ Increased levels parathyroid hormone (PTH),⁷ osteoclastic activity of the renin-angiotensin-aldosterone system⁸ and decreased serum ghrelin levels were responsible for this situation.⁹

Although there are several studies^{3,9,10} demonstrating the relationship among menopause, HT and osteoporosis in women, no study has been performed thus far to assess the relationship between osteoporosis and ambulatory blood pressure. The purpose of this study is to determine the effects of osteoporosis in postmenopausal women on circadian blood pressure assessed by ABPM.

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METHODS

The study was carried out with the permission of Erzurum Province Training and Research Hospital Ethics Committee (Date: 04.02.2011, Decision No: 417). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Patient Population

A total of 68 consecutive women patients with postmenopausal HT, who were admitted to the cardiology department of our hospital, were prospectively evaluated. Patients fulfilling the following criteria were included in the study: (i) being post-menopausal; (ii) no previous diagnosis of osteoporosis; and (iii) hypertensive and/or antihypertensive drug use. The exclusion criteria were: coronary or peripheral artery disease, heart failure, valve disease, arrhythmia, chronic diseases (renal, hematologic, inflammatory, hepatic, malignancy), thyroid dysfunction, alcohol use, secondary HT, medication associated with bone metabolism (e.g anti-osteoporotic, steroid, hormone replacement therapy, statin and warfarin), history of bone fractures and inconvenient sleep durations (<6 h or >12 h).

Ambulatory Blood Pressure Monitoring

Twenty-four hour ABPM was conducted by a Tracker NIBP2 device (del Mar Reynolds, Hertford, UK). The average 24-hour, daytime and nighttime blood pressures (systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean blood pressure (MBP)) were evaluated in all patients. An appropriate cuff size was selected for each subject. Daytime was defined as 07:00-23:00 h and nighttime was defined as 23:00-07:00 h. Measurements were performed at 15- and 30-minute intervals during the day and night, respectively. Measurements were not considered valid if SBP was <70 mmHg or >250 mmHg, DBP <40 mmHg or >150 mmHg, or PP < 10 mmHg. The patients sleeping and awake times were recorded and total sleep duration was calculated. The nocturnal fall rates of SBP, DBP and MBP were calculated according to the following formula:^{1,11} the rate of fall in night (%) = (daytime BP - nighttime BP) × 100/ daytime BP). Patients with 10-20% rate of fall in night of MBP were classified with DHT (n=34), while patients with <10% were classified with NDHT (n=34).¹²

Measurement of Bone Metabolism By Dual X Ray Absorptiometric (DXA)

Bone metabolism was measured using a whole body DXA scanner (Hologic QDR-2000, Bedford, MA, USA). Bone mineral density (BMD) was measured in all patients at the lumbar spine (L1-4) with a coefficient of variation of 0.8% and <1.2%, respectively. Bone mineral density (g/cm²) for each subject was calculated by dividing the amount of bone mineral content by the projected area

of the region of interest. Results were also expressed as a T-score (defined as the number of standard deviations [SDs] below the mean value of young women) and as Z-score (defined as the number of SDs below the mean for women of the same age). Women with a T-score < -2.5 were considered osteoporotic.⁸

Data Sources and Definitions

Blood pressure was measured at the clinics on the day of admittance and the following week, and the mean value of these two measurements was taken as the office blood pressure. Patients were accepted as hypertensive if the following were present: 1) systolic pressure was >140 mmHg and/or diastolic pressure was > 90 mmHg in office; 2) current use antihypertensive medication; or 3) average 24 h BP value above 130/80 mmHg by ABPM.² Neck circumference (NC) was measured at the midpoint of the neck between the mid-cervical spine and the mid-anterior neck 0.5 cm below the laryngeal prominence.¹³ Waist circumference (WC) was measured in a standing position after normal expiration, midway between the lower rib margin and the iliac crest.¹⁴ Transthoracic echocardiography for left ventricular mass index and epicardial fat thickness was performed using a system V (Vingmed, GE, Horten, Norway) with a 2.5-MHz phased-array transducer. Left ventricular mass index was calculated by the recommended formulas in the literature.¹⁵ Epicardial fat thickness was measured on the free wall of the right ventricle at the end-diastole using both parasternal long and short axis views on M-mode echocardiography in three cardiac cycles.¹⁶ A woman was considered to be postmenopausal if she did not report having a menstrual period within the past 12 months (provided that it is not associated with a gynecological disease).³ Metabolic syndrome was diagnosed according to the National Cholesterol Education Program Adult Treatment Panel III criteria. Any patient can be diagnosed with Metabolic syndrome when any three of the following criteria are present:¹⁷

High WC, whose thresholds depend on populations and countryspecific definitions (≥102 cm and ≥88 cm for European men and women respectively);¹⁸

- Blood TG ≥ 150 mg/dl;
- Blood HDL cholesterol < 40 mg/dl in men and
- Blood fasting glucose ≥ 100 mg/dl.

Statistical Analysis

Quantitative variables were expressed as mean value ± SD, and qualitative variables were expressed as percentages (%). A comparison of parametric values between two groups were performed by means of two-tailed student's t-test. Categorical variables were compared by the likelihood-ratio χ^2 test or Fisher's exact test. Pearson's correlation coefficients examined the degree of association between examined variables. A P value <0.05

was considered as significant. The receiver operating characteristics (ROC) curve was used to demonstrate the sensitivity and specificity of lumbar spine BMD, optimal cut-off value for predicting NDHT in patients, and postmenopausal HT. The effects of different variables on NDHT was calculated in the univariate analysis for each. The variables for which the unadjusted p value was <0.10 in the logistic regression analysis were identified as potential risk markers and included in the full model. The model was reduced by using backward elimination multivariate logistic regression analyses, and potential risk markers were eliminated using likelihood ratio tests. Confidence interval (CI) was 95%. All statistical studies were carried out with SPSS package program (version 15.0, SPSS, Chicago, Illinois, USA)

RESULTS

Baseline characteristics are shown in **Table 1**. The NDHT group was older than DHT group. The rate of \geq five years of antihypertensive drug use was higher the NDHT group ($P=0.04$). While 95.5% of the patients was using an antihypertensive drug, the ratio of using more than two drugs (combination therapy) among these patients was 5.8%.

	Dipper hypertension (n= 34)	Non-dipper hypertension (n=34)	P value
Age, y	58.8 \pm 6.6	63.3 \pm 10	0.03
Height, cm	154.2 \pm 7	153.7 \pm 6.9	0.74
Weight, kg	78.9 \pm 9.7	78 \pm 14.8	0.77
Neck circumference, cm	34.7 \pm 2.1	34.8 \pm 2.2	0.91
Waist circumference, cm	79.7 \pm 11.8	83.2 \pm 17.5	0.32
Diabetes mellitus	6 (17.6)	8 (23.5)	0.54
Hyperlipidemia	19 (55.8)	23 (67.6)	0.31
Family history for hypertension	17 (50)	10 (29.4)	0.12
Current smoker	3 (8.8)	2 (5.8)	0.64
Metabolic syndrome	32 (94.1)	28 (82.3)	0.13
Hypertension time, y	5 \pm 4.4	6.1 \pm 4.4	0.28
Medication time for hypertension			0.04
<5 Year	20 (58.8)	12 (35.2)	
\geq 5 Year	14 (41.1)	22 (64.7)	
Only β -blocker use	4 (11.7)	5 (14.7)	0.72
Only ACE-I use	12 (35.2)	7 (20.5)	0.17
Only ARB use	11 (32.3)	12 (35.2)	0.79
Only diuretics use	1 (2.9)	0 (0)	0.31
Only CCB use	4 (11.7)	5 (14.7)	0.72
Combined drug use	1 (2.9)	3 (8.8)	0.3
Left ventricular mass index, g/m ²	79 \pm 17.4	79.7 \pm 18.6	0.88
Epicardial fat thickness, mm	5.8 \pm 1.6	5.6 \pm 1.7	0.66

Mean values (SD) and % (n) are reported for continuous and categorical variables, respectively. ACE-I: Angiotensin Converting Enzyme Inhibitor, ARB:Angiotensin Receptor Blocker, CCB: Calcium Channel Blocker

With respect to baseline laboratory status (**Table 2**), there was no significant difference lipid profile, glucose level, uric acid and mean platelet volume (MPV) between groups. The red cell distribution width (RDW) value was significantly higher in non-dipper patients than in the dipper patients.

	Dipper hypertension (n= 34)	Non-dipper hypertension (n=34)	P value
Creatinine, mg/dl	0.6 \pm 0.1	0.7 \pm 0.2	0.27
Glucose, mg/dl	128.2 \pm 67	113.3 \pm 34.3	0.25
Total cholesterol, mg/dl	212.2 \pm 38.5	200.5 \pm 46.1	0.25
LDL cholesterol, mg/dl	129.2 \pm 47.8	120.6 \pm 46	0.45
HDL cholesterol, mg/dl	46 \pm 14.5	48.5 \pm 24.4	0.61
Triglycerides, mg/dl	154.5 \pm 66.6	152.8 \pm 60.1	0.91
Hemoglobin, g/dl	13.7 \pm 0.8	13.5 \pm 1.3	0.4
RDW,%	10.9 \pm 0.63	11.4 \pm 0.8	0.01
MPV,fl	8.1 \pm 1	8.1 \pm 0.97	0.99
Uric acid, mg/dl	4.1 \pm 0.8	4.6 \pm 1.4	0.09

Mean values (SD) are reported for continuous variables. LDL: Low-density lipoprotein, HDL: High-density lipoprotein, RDW: Red cell Distribution Width, MPV: Mean Platelet Volume

The results of ABPM and DXA for both groups are shown in **Table 3**. With respect to ABPM, there was no significant difference in SBP and DBP (day, night, 24 h). Total sleep duration was similar between the two study groups. Non-dipper patients had a longer duration of menopause than dipper patients and osteoporosis was more common in this patient group (50% vs 20.5%; $p=0.01$, respectively). Lumbar spine BMD was lower in non-dipper patients.

	Dipper hypertension (n= 34)	Non-dipper hypertension (n=34)	P value
Sleep time, h	8 \pm 1.2	8.2 \pm 1.6	0.74
Average day-time SBP, mmHg	138.9 \pm 11.3	134 \pm 17.6	0.27
Average night-time SBP, mmHg	122.9 \pm 11.5	130.6 \pm 19.6	0.05
Average 24-hour SBP, mmHg	134.2 \pm 10.5	133.7 \pm 18	0.8
Average day-time DBP, mmHg	92.3 \pm 10.4	89.5 \pm 15.4	0.38
Average night-time DBP, mmHg	76 \pm 8.5	79 \pm 10.6	0.14
Average 24-hour DBP, mmHg	87.6 \pm 9.1	84 \pm 10.6	0.15
Average day-time MBP, mmHg	108.4 \pm 10.9	105.9 \pm 13.1	0.39
Average night-time MBP, mmHg	91.2 \pm 9.7	96.5 \pm 13.2	0.06
Average 24-hour MBP, mmHg	104.1 \pm 12.2	100.6 \pm 12.7	0.25
Nocturnal fall in SBP, %	11.1 \pm 3.9	3.8 \pm 3.6	<0.0001
Nocturnal fall in DBP,%	17.9 \pm 6	7.7 \pm 7.4	<0.0001
Nocturnal fall in MBP,%	16.2 \pm 3.7	4.5 \pm 4.3	<0.0001
Office SBP, mmHg	139.4 \pm 12.3	140.5 \pm 19.1	0.76
Office DBP, mmHg	79.6 \pm 6	80.9 \pm 8.6	0.48
Office heart rate, beats/min	81.7 \pm 8.1	81.4 \pm 10.6	0.9
Post-menopausal time,y	10.6 \pm 7.9	15.7 \pm 10.33	0.02
Osteoporosis	7 (20.5)	17 (50)	0.01
Lumbar spine BMD, gr/cm ²	1 \pm 0.13	0.91 \pm 0.11	0.004
Lumbar spine T score, SD	-1.5 \pm 1	-2.2 \pm 0.94	0.003

Mean values (SD) and % (n) are reported for continuous and categorical variables, respectively. ABPM: Ambulatory Blood Pressure Monitoring, DXA: Dual X-ray Absorptiometric, SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure, MBP: Mean Blood Pressure, BMD: Bone mineral density

There was a significant correlation between the rate of fall in night of MBP and both lumbar spine T-score and lumbar spine BMD ($r= 0.330$ and $P=0.006$ vs $r=0.322$ and $P=0.007$, respectively). Interestingly, the rate of the fall in night for SBP and both BMD and T-score was not significantly correlated (Table 4, Figure 1).

Table 4. Correlation (r) between densitometric features of bone's and the rate (%) of fall in night of BP's

		r value	P value
MBP	Lumbar spine T-score	0.330	0.006
	Lumbar spine BMD	0.322	0.007
SBP	Lumbar spine T-score	0.208	0.09
	Lumbar spine BMD	0.204	0.09
DBP	Lumbar spine T-score	0.203	0.09
	Lumbar spine BMD	0.204	0.09

Abbreviations: MBP: Mean Blood Pressure, SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure, BMD: Bone mineral density

The ROC curves of lumbar spine BMD for predicting NDHT are shown in Figure 2. Lumbar spine BMD $<0.944\text{g/cm}^2$ measured had a 64.7% sensitivity and 64.7% specificity in predicting of NDHT. When we divided the study population into two groups (Table 5) according to the $<0.944\text{g/cm}^2$ lumbar spine BMD cut-off value used in the ROC analysis, NDHT and age were significantly higher in the low lumbar spine BMD group. While the low spine BMD group had lower height and NC, they had higher weight and WC. Office and daytime DBP was lower in the low lumbar spine BMD group, while there was no difference between the groups with respect to other blood pressures. The rate of fall in night of MBP was significantly lower in low lumbar spine BMD group; however this significance was not observed for SBP or DBP. Echocardiographic findings indicating LV remodeling were similar between the two groups,

whereas epicardial fat thickness significantly increased in the high lumbar spine BMD group.

An unadjusted p value < 0.10 in the univariate analysis was identified as a potential risk marker for NDHT and was included in the full model. Age >65 y, hypertension duration (>5 y), glucose, HbA1c, RDW, high uric acid (≥ 6 mg/dl), weight, low lumbar spine BMD, post-menopausal time, height, NC, WC and epicardial fat thickness were analyzed using a multivariate logistic regression model. At the multivariate analyses, hypertension duration (>5 y), RDW, high uric acid ($\geq 6\text{mg/dl}$) and low lumbar spine BMD (odds ratio=6.13, 95% confidence interval:1.2-30.6, $p=0.02$) were still independent predictors of NDHT (Table 6).

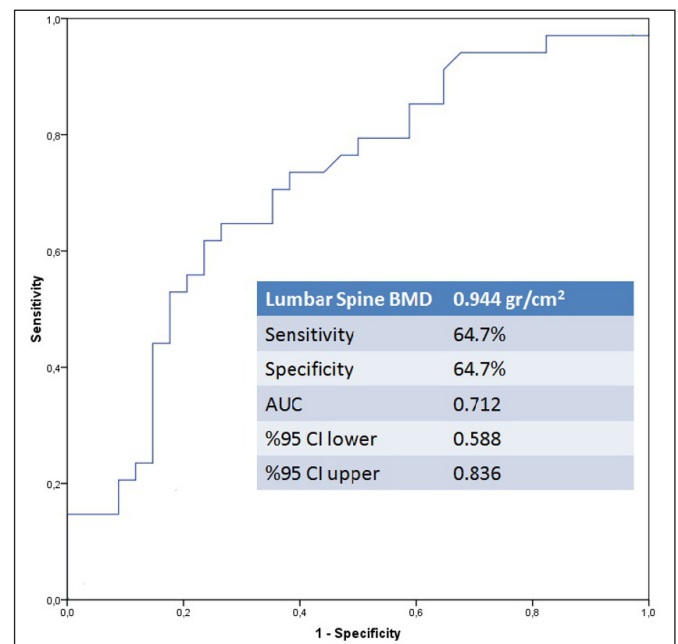


Figure 2. The receiver-operating characteristic (ROC) curve of lumbar spine BMD for predicting non - dipper hypertension (BMD: Bone mineral density, AUC: area under curve, CI: confidence interval)

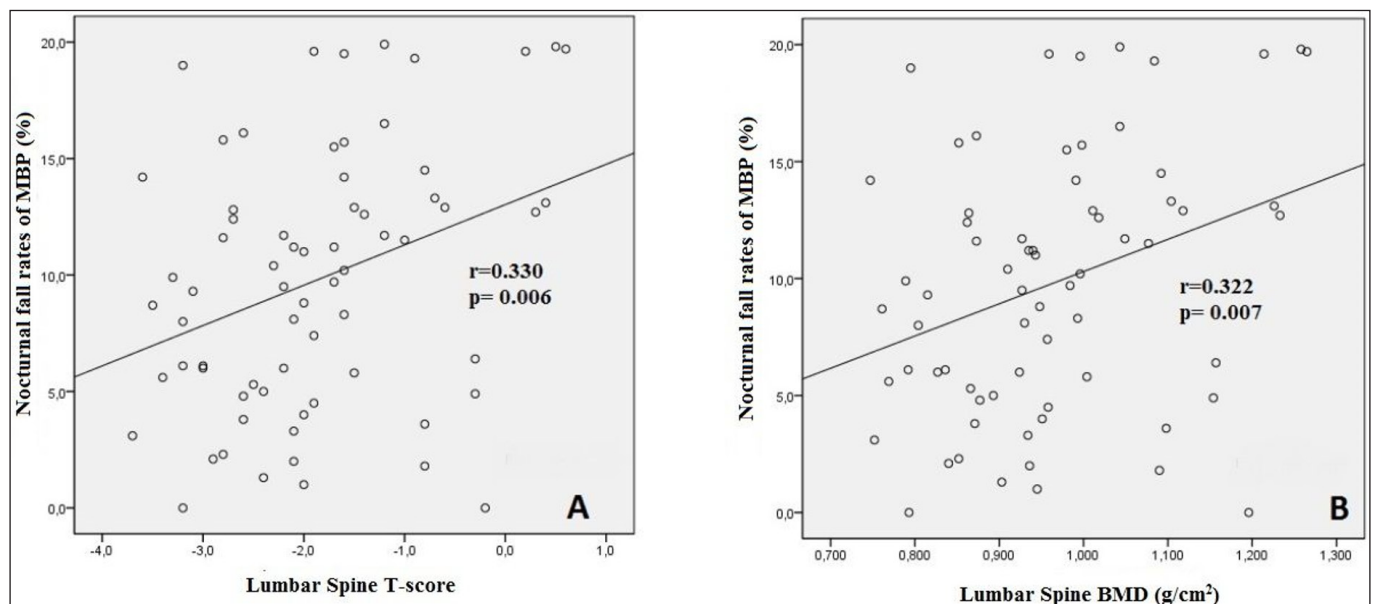


Figure 1. Relation of the rate (%) of fall in night of MBP with lumbar spine T - score (A) and lumbar spine BMD (B) in a scatter figures (MBP: Mean blood pressure, BMD: Bone mineral density)

Table 5. The results of patients stratified by lumbar spine BMD

	High lumbar spine BMD (n =34)	Low lumbar spine BMD (n= 34)	P value
Age, y	56.7±5.7	65.4± 9.1	<0.001
Diabetes mellitus	9 (26.4)	5(14.7)	0.23
Current smoker	2 (5.8)	3 (8.8)	0.64
Family history for hypertension	17 (50)	10 (29.4)	0.22
Hypertension time,y	6.1±4.7	5.2±4.1	0.47
Medication time for hypertension			0.33
<5 Year	16 (47)	19 (55.8)	
≥5 Year	18 (53)	15 (44.1)	
Height, cm	155±7	152.3±7.3	0.04
Weight, kg	74.2±12	82.7±11.6	0.004
Neck Circumference, cm	35.4±2.2	34±1.7	0.007
Waist Circumference, cm	80.6±9.5	90.9±11.2	<0.001
Only Diuretics use	0 (0)	1(2.9)	0.31
Only ACE-I use	10 (29.4)	9 (26.4)	0.78
Only ARB use	11 (32.3)	12 (35.2)	0.79
Combine drug use	1 (2.9)	3 (8.8)	0.3
Average day-time SBP, mmHg	140.1±11.7	133.6±16.9	0.07
Average night-time SBP, mmHg	127.8±16	125.8±17.1	0.62
Average 24-hour SBP, mmHg	136.5±11.8	131.5±16.8	0.16
Average day-time DBP, mmHg	91.7±10.1	86±11.7	0.03
Average night-time DBP, mmHg	79±9.6	76.7±9.8	0.34
Average 24-hour DBP, mmHg	88±8.9	83.7±10.6	0.07
Average day-time MBP, mmHg	106.4±10.7	104.9±13	0.46
Average night-time MBP, mmHg	94.9±11.9	93±11.8	0.53
Average 24-hour MBP, mmHg	105.1±12.3	99.6±12.3	0.07
Office SBP, mmHg	141.3±14.4	138.6±17.5	0.48
Office DBP, mmHg	82.4±6.3	78.1±7.9	0.01
Nocturnal fall in SBP, %	8.4±6.3	5.8±5	0.06
Nocturnal fall in DBP,%	14±9.1	10.5±6.7	0.07
Nocturnal fall in MBP,%	13±6.3	7.8±5.6	0.001
Non-dipper hypertension	12 (35.2)	22 (64.7)	0.01
Lumbar spine T score, SD	-1.04±0.79	-2.7±0.51	<0.001
Post-menopausal time,y	8.4±7.1	17.9±9.2	<0.001
Left ventricular mass index, g/m ²	78.1±18	80.6±17.9	0.58
Epicardial fat thickness, mm	6.2±1.8	5.3±1.2	0.02

Mean values (SD) and % (n) are reported for continuous and categorical variables, respectively. ACE-I: Angiotensin Converting Enzyme Inhibitor, ARB:Angiotensin Receptor Blocker, SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure, MBP: Mean Blood Pressure, BMD:Bone mineral density, RDW: Red cellDistribution Width, MPV: Mean Platelet Volume

Table 6. Effects of various variables on non-dipper hypertension in univariate and multivariate logistic regression analyses

Variables	Univariate OR	% 95 CI	P value	Multivariate OR	% 95 CI	P value
Age	1.067	1.003-1.135	0.04	-	-	-
Age >65 years	2.012	0.703-5.76	0.193	-	-	-
Hypertension time (>5 y)	2.96	1.104-7.942	0.03	4.542	1.126-18.325	0.03
Glucose	0.994	0.984-1.005	0.25	-	-	-
Hemoglobin A1c	0.805	0.469-1.379	0.42	-	-	-
RDW	0.28	0.103-0.78	0.016	4.809	1.161-19.912	0.03
Uric acid (>6 mg/dl)	7.07	0.803-62.311	0.07	27.89	1.32-121.82	0.03
Weight	0.994	0.95-1.033	0.77	-	-	-
Low lumbar spine BMD	3.36	1.2-9.08	0.017	6.13	1.2-30.6	0.02
Post-menopausal time	1.063	1.006-1.123	0.02	-	-	-
Neck circumference	1.013	0.8-1.27	0.91	-	-	-
Height	0.98	0.92-1.059	0.74	-	-	-
Waist circumference	1.03	0.98-1.08	0.32	-	-	-
Epicardial fat thickness	0.52	0.2-9.3	0.66	-	-	-

OR: odds ratio, CI: confidence interval, RDW: red cell distribution width, BMD:Bone mineral density

DISCUSSION

This study includes three major findings in patients with postmenopausal HT: i) osteoporosis is more common in patients with NDHT; ii) NDHT frequency is higher in patients with low lumbar spine BMD; and iii) lumbar spine BMD <0.944 g/cm² is an independent risk factor for NDHT.

Impairment in the circadian rhythms of bone tissue and blood pressure as seen with menopause increases the incidence of osteoporosis and HT.^{3,5} These two diseases are associated with mortality and morbidity.⁶ Physiologically, the osteoblastic and osteoclastic activities of the bones are in an equilibrium and osteoclastic activity is greater during the night than during the day.¹⁹

The most interesting finding of this study is that NDHT was more frequent in the patients with low lumbar spine BMD, which to our knowledge, this is the first study to report an association between osteoporosis and NDHT. This clinical coexistence may be explained by four pathophysiological mechanisms that blunted the nocturnal decline in blood pressure as well as increase in bone loss during nighttime. First, PTH; the physiological rhythmic secretion of this hormone which is associated with HT is impaired in osteoporotic patients.^{20,21} In patients with low BMD reaches peak levels between 02.00-11.00 a.m. compared to patients with normal BMD.⁷ Secondly; plasma melatonin and ghrelin levels, which are physiologically expected to be elevated during nighttime, however have reduced serum levels in osteoporotics.^{9,22} In addition to their osteoblastic properties, these two hormones are also known to have positive effects on cardiovascular tissues and it was demonstrated that a decrease in serum levels of these hormones is a risk factor for NDHT.^{9,22} In patients with excessive sodium consumption, a negative correlation was noted between urine sodium/creatinin ratio and BMD. As known, excessive sodium consumption is one of the possible causes of NDHT.¹⁰ Fourthly, autonomous system disorders worth mentioning. Hyperactivation of the sympathetic system during the night is known to increase bone resorption and the frequency of NDHT.²³ Due to the above mentioned four reasons, on one hand osteoclastic activity is maintained and on the other hand, a decrease in blood pressure will be inadequately during the night.

Gunebakmaz O et al.²⁴ demonstrated that increased RDW levels in patients with NDHT and they have shown a negative correlation between the rate of nocturnal fall in SBP and RDW. However, Afsar B et al.²⁵ determined that a high level of uric acid is an independent marker of NDHT. Although no relation between osteoporosis and RDW levels has been reported thus far in the literature,

it is argued that high uric acid levels may be protective against osteoporosis.²⁶ Our findings showed that the uric acid levels were similar between the two groups in this study. We have observed that RDW and high uric acid level may be among the independent markers of NDHT. Although the relation between RDW or high uric acid level and hypertension has not yet been completely understood, this may be considered to be associated with the increased inflammatory response and oxidative stress in this group of patients.^{24,25}

In the current study, we observed that patients with high lumbar BMD had increased NC and epicardial fat thickness; according to the literature²⁷ this condition has the closest clinical association with obstructive sleep apnea. Sforza E et al.¹³ demonstrated that in patients with obstructive sleep apnea, apnea-related intermittent hypoxia induces bone remodeling process. Our findings indicated that patients with high lumbar BMD had high NC and epicardial fat thickness may be associated with obstructive sleep apnea.

Limitations of the Study

Several limitations should be taken into consideration while assessing the results of this study. First, only a small number of patients from one center were enrolled. However, in the case of postmenopausal women, the patient ratios for HT and osteoporosis were similar (50% and 50%, respectively) with previous studies.^{3,9,25} Secondly, parameters that are biochemical markers of bone turnover (such as calcium) and plasma renin activity, PTH, ghrelin, and melatonin, all of which effect bone turnover, were not assessed in this study. Thirdly, keeping in mind that the HT induced osteoporosis develops in the target organ damage and activity of the renin-angiotensin-aldosterone system, we might have underestimated the prevalence of osteoporosis because of some of the patients were using antihypertensive medications. Further information can be provided on this subject by extensive studies performed on large patient populations.

CONCLUSION

In patients with postmenopausal HT, the decrease in lumbar spine BMD increases the frequency of NDHT. Therefore, the detection of osteoporosis in postmenopausal hypertensive women may be a predictor of cardiovascular risk.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Erzurum Province Training and Research Hospital Ethics Committee (Date: 04.02.2011, Decision No: 417).

Informed consent: Written consent was obtained from the patient participating in this study.

Referee Evaluation Process: Externally peer reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Author Contributions: All the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

- Kaya MG, Yarlioglu M, Gunebakmaz O, et al. Platelet activation and inflammatory response in patients with non-dipper hypertension. *Atherosclerosis*. 2010;20(1):278-282.
- Mancia G, Fagard R, Narkiewicz K, et al. 2013 ESH/ESC guidelines for the management of arterial hypertension: the Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *Eur Heart J*. 2013;34(28):2159-2219.
- Routledge FS, McFetridge-Durdle JA, Dean CR. Stress, menopausal status and nocturnal blood pressure dipping patterns among hypertensive women. *Can J Cardiol*. 2009;25(6):157-163.
- Pusuroglu H, Cakmak HA, Erturk M, et al. Assessment of the relation between mean platelet volume, non-dipping blood pressure pattern and left ventricular mass index in sustained hypertension. *Med Sci Monit*. 2014;20:2020-2026.
- Frost ML, Grella R, Millasseau SC, et al. Relationship of calcification of atherosclerotic plaque and arterial stiffness to bone mineral density and osteoprotegerin in postmenopausal women referred for osteoporosis screening. *Calcif Tissue Int*. 2008;83(2):112-120.
- Cappuccio FP, Meilahn E, Zmuda JM, Cauley JA. High blood pressure and bone-mineral loss in elderly white women: a prospective study. Study of Osteoporotic Fractures Research Group. *Lancet*. 1999;354(9183):971-975.
- White HD, Ahmad AM, Durham BH, et al. PTH circadian rhythm and PTH target-organ sensitivity is altered in patients with adult growth hormone deficiency with low BMD. *J Bone Miner Res*. 2007;22(11):1798-1807.
- Asaba Y, Ito M, Fumoto T, et al. Activation of renin-angiotensin system induces osteoporosis independently of hypertension. *J Bone Miner Res*. 2009;24(2):241-250.
- Pérez-Castrillón JL, Justo I, Sanz A, et al. Ghrelin and bone mass in postmenopausal hypertensive women. *Ann Nutr Metab*. 2007;51(3):223-227.
- Woo J, Kwok T, Leung J, Tang N. Dietary intake, blood pressure and osteoporosis. *J Hum Hypertens*. 2009;23(7):451-455.
- Turfaner N, Karter Y, Curgunlu A, Ayan F, Mihmanli I, Sipahioglu F. Blunted nocturnal fall of blood pressure in isolated clinical hypertension. *Swiss Med Wkly*. 2009;139(17-18):251-255.
- Aydin M, Ozeren A, Bilge M, Dursun A, Cam F, Elbey MA. Effects of dipper and non-dipper status of essential hypertension on left atrial mechanical functions. *Int J Cardiol*. 2004;96(3):419-424.
- Sforza E, Thomas T, Barthélémy JC, Collet P, Roche F. Obstructive sleep apnea is associated with preserved bone mineral density in healthy elderly subjects. *Sleep*. 2013;36(10):1509-1515.
- Dahlén EM, Bjarnegård N, Länne T, Nyström FH, Ostgren CJ. Sagittal abdominal diameter is a more independent measure compared with waist circumference to predict arterial stiffness in subjects with type 2 diabetes—a prospective observational cohort study. *Cardiovasc Diabetol*. 2013;12:55.
- Schiller NB, Shah PM, Crawford M, et al. Recommendations for quantitation of the left ventricle by two-dimensional echocardiography. American Society of Echocardiography Committee on Standards, Subcommittee on Quantitation of Two-Dimensional Echocardiograms. *J Am Soc Echocardiogr*. 1989;2(5):358-367.
- Iacobellis G, Ribaldo MC, Assael F, et al. Echocardiographic epicardial adipose tissue is related to anthropometric and clinical parameters of metabolic syndrome: a new indicator of cardiovascular risk. *J Clin Endocrinol Metab*. 2003;88(11):5163-5168.
- Kassi E, Pervanidou P, Kaltsas G, Chrousos G. Metabolic Syndrome: Definitions and Controversies. *BMC Med*. 2011;9:48.
- Alberti KGMM, Eckel RH, Grundy SM, et al. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; And International Association for the Study of Obesity. *Circulation*. 2009;120(16):1640-1645.
- Henriksen DB, Alexandersen P, Hartmann B, et al. Disassociation of bone resorption and formation by GLP-2: a 14-day study in healthy postmenopausal women. *Bone*. 2007;40:723-729.
- Fraser WD, Ahmad AM, Vora JP. The physiology of the circadian rhythm of parathyroid hormone and its potential as a treatment for osteoporosis. *Curr Opin Nephrol Hypertens*. 2004;13(4):437-444.
- Brown JM, Williams JS, Luther JM, et al. Human interventions to characterize novel relationships between the renin-angiotensin-aldosterone system and parathyroid hormone. *Hypertension*. 2014;63(2):273-280.
- Liu J, Huang F, He HW. Melatonin effects on hard tissues: bone and tooth. *Int J Mol Sci*. 2013;14(5):10063-10074.
- Tosun A, Dođru MT, Aydın G, et al. Does autonomic dysfunction exist in postmenopausal osteoporosis? *Am J Phys Med Rehabil*. 2011;90(12):1012-1019.
- Gunebakmaz O, Kaya MG, Duran M, Akpek M, Elcik D, Eryol NK. Red blood cell distribution width in 'non-dippers' versus 'dippers'. *Cardiology*. 2012;123(3):154-159.
- Afsar B, Elsurur R, Ozdemir FN, Sezer S. Uric acid and nocturnal nondipping in hypertensive patients with normal renal function. *J Nephrol*. 2008;21(3):406-411.
- Ishii S, Miyao M, Mizuno Y, Tanaka-Ishikawa M, Akishita M, Ouchi Y. Association between serum uric acid and lumbar spine bone mineral density in peri- and postmenopausal Japanese women. *Osteoporos Int*. 2014;25(3):1099-1105.
- Mariani S, Fiore D, Barbaro G, et al. Association of epicardial fat thickness with the severity of obstructive sleep apnea in obese patients. *Int J Cardiol*. 2013;167(5):2244-2249.