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Non dipping pattern frequency and metabolic syndrome relationship according to two different metabolic syndrome diagnostic methods in newly diagnosed hypertensive individuals

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ABSTRACT

Aim: The literature presents conflicting data regarding whether the non dipping pattern (NDP) in patients with metabolic syndrome (MS) compared to those without. In our study, we aimed to investigate the MS effect of the NDP in individuals with hypertension.

Methods: This prospective study included 117 newly diagnosed hypertensive patients (79 women and 38 men) who were not receiving any anti-hypertensive treatment. MS was evaluated according to the currently used the US National Cholesterol Education Programme Adult Treatment Panel-III definition criteria (MS-ATP-III) and a new diagnostic scoring method (MS-Score). NDP defined, nocturnal blood pressure (BP) fell by <10% from daytime BP

Results: The mean age of the patients who met the MS-ATP-III criteria was 53.9+8.1 years. The prevalence of the MS-ATP-III among the study population was 60.6%. The NDP frequency was similar in patients with and without MS-ATP-III, high MS-Score and low MS-Score group (respectively; 44.8%, 47.5%, p=0.79, 44.7%, 46.9%, p= 0.9). The reverse dipping pattern (RDP) frequency was higher in patients with MS-ATP-III compared to those without MS (13.8% and 2.5%, p=0.021), RDP was 10.8% in the high MS-Score group and 8.2% in the low MS-Score group (p=0.66). The LDL (mg/dL) values were higher in those with NDP compared to those without (142.6+32.2, 125.5+28.9, p=0.008).

Conclusion: Despite the high prevalence of MS among newly diagnosed hypertensive patients, the prevalence of NDP does not show a different distribution in patients with MS in both the MS-ATP-III and MS-Score method.

Keywords: Hypertension, non-dipping pattern, metabolic syndrome, reverse dipping pattern, metabolic score

INTRODUCTION

Metabolic syndrome (MS) is a cluster of factors that can increase the risk of developing cardiovascular disease, coronary artery disease, cardiovascular mortality and stroke.[1-4] In addition, a relationship between MS and clinical finding indicating organ damage, such as left ventricular hypertrophy, diastolic dysfunction and microalbuminuria, has been reported.[5-8] The normal circadian blood pressure pattern is characterised by a decrease of 10%–20% in night-time blood pressure levels compared to the daytime levels and is called the dipping pattern (DP). Various researchers have individually defined the non-dipping pattern (NDP) as a reduction of less than 10% in night-time systolic, diastolic or both blood pressure measurements.[9,10] In essential hypertensive patients, as in normotensive individuals, blood pressure levels similarly increase in the early morning hours and decrease during sleep at night. However, in some hypertensive patients, blood pressure may not decrease at night during sleep, or it may decrease slightly or even show some increase.[9-11] In the diagnosis and evaluation of arterial hypertension (HT), ambulatory blood pressure monitoring (ABPM) has been recognised as a better technique compared to office blood pressure measurement, and it works automatically by providing multiple measurements of daily activity and sleep. Consequently, it presents 24-hour (24-h) diurnal blood pressure changes.[11,12] The NDP in blood pressure may be associated with an autonomic nervous system disorder which is characterised by a decrease in parasympathetic system activity.[13] Many previous studies evaluating the relationship between the NDP in blood pressure and target organ damage have shown that the NDP is an independent predictor of left ventricular hypertrophy,

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renal dysfunction, carotid artery stenosis disease and future cardiovascular events.[7,14,15] In addition, many studies have associated the NDP with increased cardiovascular mortality and morbidity.[16,17]

Previous studies have reported controversial results regarding the relationship between MS and the disruption of the diurnal blood pressure pattern. In some of these studies, the rate of NDP and office and ambulatory blood pressure levels were significantly higher in hypertensive patients with MS.[18-21] In some studies, no relationship was found between MS and NDP.[22-25]

In this study, we aimed to investigate the circadian changes in blood pressure, especially the rate of NDP in treatment-naive hypertensive patients with and without MS.

METHODS

Patients who applied to the general internal medicine outpatient clinic between November 2008 and January 2009 were included in the study.

Inclusion Criteria

Patients who were at least 30 years old and were not receiving any anti-hypertensive treatment were included in the study.

Age-and gender-matched patients with untreated HT and without MS formed the control group.

Exclusion Criteria

Patients who were pregnant, were suffering from any chronic disease, had a history of HT treatment, under 30 years of age, suspicion of secondary HT (for example those with hypokalaemia) and refused to participate in the study were excluded. Patients who had previously taken any medication; oral contraceptives, antidepressants or corticosteroids, etc. were excluded from the study. None of the patients in the study were breastfeeding.

Study Design and Work Plan

For MS diagnosis, the US National Cholesterol Education Programme Adult Treatment Panel III (NCEP-ATP III) diagnostic criteria were used.[26] In addition to HT, at least two of the following four criteria were sought for diagnosis; I. Abdominal obesity (waist circumference >102 cm in men, >88 cm in women), II. High triglycerides (>150 mmol/L), III. Low High-density lipoprotein (HDL) cholesterol (<40 mol/L in men, <50 mol/L in women, IV. Impaired fasting glycaemia (fasting plasma glucose [FPG] >110 mg/dL, or previously diagnosed type 2 diabetes mellitus). FPG, total cholesterol, low-density lipoprotein cholesterol (LDL) cholesterol, HDL cholesterol and triglyceride levels, which were obtained from the outpatient clinic observation files.

Anthropometric measurements, waist circumference (accepted as the narrowest diameter between the arch costa and spina iliaca anterior superior), weight and height were measured, and the body mass index (BMI) was calculated (in kg/m²).

In addition, patients were classified according to the metabolic score (MS-Score) described by Macchia and colleagues[27] scoring is as follows; Male 3 points, age (year) >50 4 points, HT 2 points, BMI (kg/m²); <26 0 points, 26-27 3 points, >28 6 points, triglycerides (mg/dL); 100-159 5 points, 160-199 7 points, >200 9 points, HDL blood cholesterol (mg/dL); >50 0 points, 30-49 3 points, <30 5 points, FPG (mg/dL); <80 0 points, 80-89 5 points, 90-99 10 points, 100-109 16 points, >110 28 points, as high MS-Score if >28 points and low MS-Score if <28 points.27 According to NCEP-ATP III (MS-ATP III) and MS-Score, patients were defined as MS-ATP III (-) and low MS-Score group I, MS-ATP III (+) and low MS-Score group II, MS-ATP III (-) and high MS-Score group III, and finally MS-ATP III (+) and high MS-Score group IV.

For the patients deemed eligible to be included in the study, blood pressure was measured three times a week according to the 2007 ESH and 2008 ESC.[28,29] Before the blood pressure measurement, it was ensured that the patients had rested for at least 5 min and had not consumed coffee, tea or tobacco within half an hour. Systolic blood pressure and diastolic blood pressure were first measured in the non-dominant arm and 2 minutes later in the other arm according to Koroktoff sounds using a mercury sphygmomanometer, in the sitting position and the mean values were recorded. The mean of the three measurements within a week was considered the blood pressure level. Those with mean arterial blood pressure, systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg considered HT and included in the study. Afterwards, the patients were fitted with an ambulatory blood pressure device, and those with the 24-h mean blood pressure >130/80 mmHg, daytime mean blood pressure >135/85 mmHg, night-time mean blood pressure >120/70 mmHg, systolic and/or diastolic blood pressure were considered hypertensive. Patients were asked to sleep in the night interval and it was checked with the patients' declaration.

The non-dominant arm and the Watch BP03 device were used for 24-h blood pressure measurement in all patients. The blood pressure monitor was set to

read at 20-min intervals until 07:00–23:00 and at 30-min intervals until 23:00–07:00. All participants were encouraged to continue their routine activities upon leaving the hospital. Information on the mean systolic and diastolic blood pressure levels and heart rate for 24-h during both daytime and night-time was obtained from the records of the ambulatory blood pressure measuring device.

Nocturnal dipping is defined as a 10%–20% decrease in night-time mean systolic blood pressure compared to the daytime value. When this decrease is <10%, we define it as the NDP, and when it is >20%, we define it as extreme DP; if the night-time mean systolic blood pressure increases compared to the daytime value, it is considered as RDP.[9,10]

The IBM® Statistical Package for the Social Sciences (SPSS) statistics programme was used for the statistical evaluation of the data. After the normal distribution was determined t-test was used for comparing the normally distributed data, and a Mann–Whitney U test was conducted to compare non-normally distributed data. In the data comparison, Chi-square was used comparing the ratios, a p value of less than 0.05 was considered statistically significant.

RESULTS

A total of 117 patients, 79 female and 38 male, were identified as meeting the inclusion criteria. The mean age of the patients was 51.3+10.0 years. The prevalence of the MS among the study population was 60.6% (71) and the sex-specific prevalences were 47.4% (53) and 67.1% (18) among female and male patients respectively (p=0.041). The mean age of patients who met the MS-ATP III criterion was 53.9+8.1 years. The demographic characteristics of the patients are listed in Table 1.

NDP

While the parameters such as age, waist circumference, BMI, triglycerides and FPG were similar in patients with NDP compared to those without (Table 2), the LDL (mg/dl) values were found to be lower in those with NDP (Table 2).

The NDP frequency was 51.0% in patients with a BMI (kg/m²) below 30 and 56.5% in those with a BMI above 30, and the two groups were found to be similar (p=0.59).

When the patients were grouped into subgroups according to gender, the NDP frequency was found to be the same in both men and women with and without MS-ATP III (p=0.46, Figure 1.).

Table 1. Characteristics of patients with and without MS

	MS-ATP III (+) (n=71)	MS-ATP III (-) (n=46)	p
Age (years)	53.9+8.1	49.3+9.9	0.007
Body mass index (kg/m²)	31.3+4.7	28.7+4.7	0.003
Waist circumference (cm)	103.1+10.4	97.4+9.4	0.003
Total cholesterol (mg/dL)	201.3+38.2	204.6+40.9	0.7
Triglyceride (mg/dL)	160.0* (69.0-442.0)	113.5* (89.3-138.3)	<0.001
HDL cholesterol (mg/dL)	41.5+9.0	49.5+9.0	<0.001
LDL cholesterol (mg/dL)	135.9+30.5	130.0+32.4	0.34
Fasting blood glucose (mg/dL)	101.7+14.3	91.6+8.8	<0.001
24 hour average systolic blood pressure (mmHg)	136.1+11.2	124.5 + 13.3	<0.001
24 hour average diastolic blood pressure (mmHg)	81.9+7.2	77.5+8.6	0.005
Awake average systolic blood pressure (mmHg)	140.0+10.5	128.6+14.5	<0.001
Awake average diastolic blood pressure (mmHg)	85.2+7.2	80.9+9.3	0.008
Asleep average systolic blood pressure (mmHg)	125.5+15.1	113.4+13.9	<0.001
Asleep average diastolic blood pressure (mmHg)	73.7+9.9	70.4+9.7	0.092
24 h average pulse pressure (mmHg)	54.1+9.0	47.0 + 9.1	<0.001
Awake pulse pressure (mmHg)	54.7+9.1	47.7+9.9	<0.001
Asleep pulse pressure (mmHg)	40.3+14.7	32.5+12.1	0.005
NDP frequency (%)	44.8	47.5	>0.79

MS-ATP III: Metabolic syndrome according to the National Cholesterol Education Programme Adult Treatment Panel III, HDL: High-density lipoprotein cholesterol, LDL: Low-density lipoprotein cholesterol, NDP: Non dipping pattern, *since it does not show normal distribution, it is given as median and interquartile range of 25–75 percentiles.

Table 2. Demographic characteristics by dipping pattern and non-dipping pattern

	NDP (n=54)	DP (n=63)	p
Age (years)	52.6+9.5	53.2+8.6	0.56
Body mass index (kg/m²)	31.6+4.9	31.3+5.3	0.83
Waist circumference (cm)	103.0+ 8.5	102.3+11.3	0.88
Total cholesterol (mg/dL)	202.7+38.2	208.8 + 40.4	0.72
Triglyceride (mg/dL)	153.7* (98.5-182.0)	143.0* (108.5-178.0)	0.63
HDL cholesterol (mg/dL)	40.6+11.7	46.6+11.7	0.79
LDL cholesterol (mg/dL)	126.3 + 28.6	141.4+32.9	0.008
Fasting blood glucose (mg/dL)	95.8+12.5	98.6+15.6	0.53

DP: Dipping pattern, NDP: Non dipping pattern,HDL: High-density lipoprotein cholesterol, LDL: Low-density lipoprotein cholesterol, *since it does not show normal distribution, it is given as median and interquartile range of 25–75 percentiles.

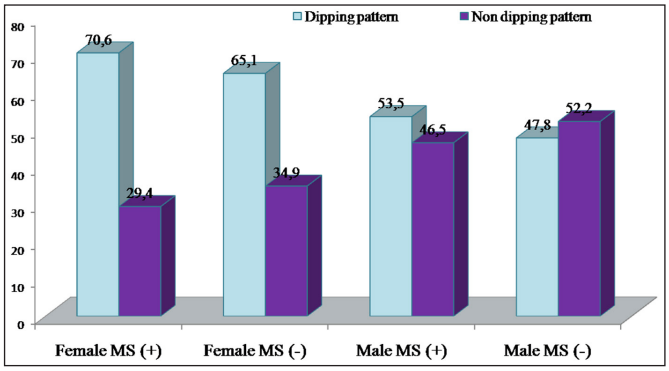

Figure 1. Non dipping pattern frequency according to gender and metabolic syndrome (MS), with and without MS equal distribution for both genders is observed (Female p=0.66, male p=0.9).

The NDP frequency was 50% in patients who did not meet any of the metabolic ATP III diagnostic criteria other than HT, 42.9% in those who met one criterion other than HT, 40.9% in those who met two criteria other than HT, 33.3% in those who met three criteria other than HT,39.1% in those who met four criteria thus, the differences were not significant.

RDP

The RDP frequency was higher in patients with MS-ATP III compared to those without MS-ATP III (13.8% and 2.5%, respectively; p =0.021). While the RDP was seen as 13.5% in men, no RDP was observed in women (p =0.028). When the patients were classified as below and above 30 according to their BMI (kg/m²), the RDP was 2% in those below 30 of BMI and 17.4% in those above 30 BMI (p=0.009).

Extreme DP

Extreme DP was detected as 10.3% in patients with MS-ATP III and 10.0% in those without MS-ATP III; the two groups were similar. In addition, it was found to be 9.1% in women, 12.5% in men, 7.8% in those with a BMI below 30, 13% in those with a BMI above 30, 9.1% in those under 45 years of age and 14.3% in those above 45 years of age. The groups were found to be similar. Patients with extreme DP were also found to be similar in age, BMI and metabolic parameters compared to those without DP.

According to the MS-Score

The characteristics of the patients according to their MS-Score are shown in Table 2. The frequency of NDP was similar in the group with high and low MS-Score (Table 3). In addition, when group I was compared with group IV in terms of NDP frequency, it was also similar (Figure 2). The frequency of RDP was 10.8% in the high MS-Score group and 8.2% in the low MS-Score group (p=0.66).

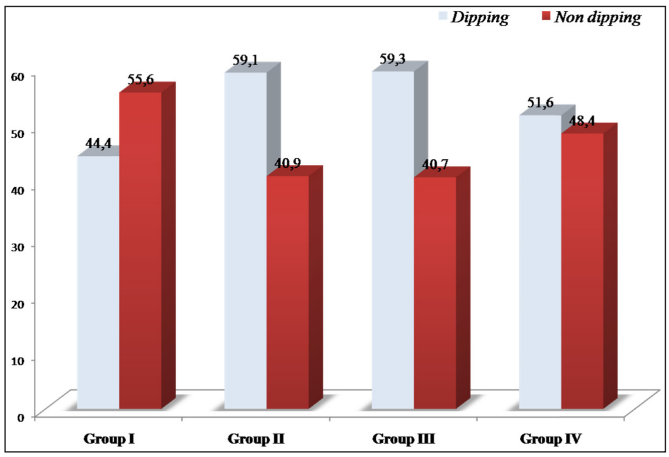

Figure 2. Non dipping pattern frequency according to both MS diagnostic methods, non dipping pattern is found to be similar distribution in groups (from I to IV).

Table 3. Characteristics of patients with high MS-Score and low MS-Score

	MS-Score high (n=54)	MS-Score low (n=62)	p
Age (years)	54.2+7.0	49.1+11.3	0.004
Female/Male (n)	33/21	46/16	0.29
Body mass index (kg/m²)	31.9+4.4	28.8+4.3	<0.001
Waist circumference (cm)	104.6+10.7	96.8+9.8	<0.001
Total cholesterol (mg/dL)	191.0+37.1	214.3+38.2	0.011
Triglyceride (mg/dL)	153.5* (69.0-442.0)	115.0* (48.0-341.0)	<0.001
HDL cholesterol (mg/dL)	42.1+8.1	46.9+11.1	0.009
LDL cholesterol (mg/dL)	131.9+26.5	135.9+35.8	0.5
Fasting blood glucose (mg/dL)	107.6+11.8	88.9+7.6	<0.001
24 hour average systolic blood pressure (mmHg)	134.9+13.9	128.6+12.3	0.017
24 hour average diastolic blood pressure (mmHg)	82.4+7.7	78.1+7.9	0.005
Awake average systolic blood pressure (mmHg)	138.6+13.5	132.5+12.9	0.018
Awake average diastolic blood pressure (mmHg)	85.5+7.4	81.4+8.4	0.008
Asleep average systolic blood pressure (mmHg)	1245+164	117.9+14.9	0.032
Asleep average diastolic blood pressure (mmHg)	74.1+10.3	70.9+9.6	0.10
24 h average pulse pressure (mmHg)	52.4+10.2	50.6+9.2	0.32
Awake pulse pressure (mmHg)	53.1+10.3	51.3+9.8	0.36
Asleep pulse pressure (mmHg)	38.9+14.4	36.2+14.2	0.34
NDP frequency (%)	44.7	46.9	0.9

MS-Score: Metabolic score described by Macchia and colleagues [27], HDL: High-density lipoprotein cholesterol, LDL: Low-density lipoprotein cholesterol, NDP: Non dipping pattern,*since it does not show normal distribution, it is given as median and interquartile range of 25–75 percentiles.

DISCUSSION

In our study, we found that the prevalence of MS was high in newly diagnosed hypertensive patients who were not receiving any anti-hypertensive treatment. There was no difference in NDP between the MS and non-MS groups. When we investigated the relationship between MS and non-dipping blood pressure by comparing different MS definitions, the frequency of NDP was similar between patient groups in both different MS diagnostic methods. The frequency of RDP was higher in patients with MS-ATP III, but not in those with high scores according to MS-Score.

One of the main results of our study is that the frequency of the non-dipping blood pressure pattern was not higher in patients with MS-ATP III. Cuspidi et al.[5,22] Bastos et al.[23] and Foss et al.[22] found that the 24-h average systolic blood pressure (ASBP), awake average systolic blood pressure (AASBP) and asleep average systolic blood pressure (AsASBP) levels were similar for the patients with and without MS.[5,22-24] In the same studies,

the NDP frequency was found to be similar in patients with and without MS.[5,22,23,24] Unlike previous studies, Mancia et al.[25] found that systolic and diastolic blood pressure measurements performed in the office, at home and in ambulatory care for patients with MS were higher than those without MS, while the diurnal variation between wakefulness and night-time was preserved.[25] We observed similar results in our study, where ASBP, AASBP and AsASBP values were higher in patients with MS-ATP III, but the diurnal blood pressure difference was the same between the two groups. A study group of 2,045 non-diabetic patients with a mean age of 49.4 years, who had not received antihypertensive treatment before, was examined by Ayala et al.[18] who found that the 48-h mean systolic/diastolic blood pressure, daytime waking mean systolic or diastolic blood pressure, night-time mean systolic blood pressure, 48-h mean pulse pressure, wakefulness mean pulse pressure and night-time mean pulse pressure were higher in patients with MS than in those without MS.[18] In this respect, our study is similar to Ayala et al's[18] study but differs in that we found the NDP frequency not to be higher in the patient group with MS-ATP III. One of the largest-scale studies that found an association between MS and NDP is the study by Ayala et al.[18] their work is in some aspects different from our work. The frequency of male participants was significantly higher in patients with MS, as a result, the reason for the lower frequency of NDP in patients with MS in the study of Ayala et al.[18] may be that the two groups were not matched in terms of age and gender.[18]

In addition, we found that pulse pressure was higher in patients with MS-ATP III . High pulse pressure is detected when systolic pressure rises or diastolic pressure falls. Epidemiological studies have shown that high pulse pressure is associated with increased systolic HT and cardiovascular events.[30,31] For example, Blacher et al.[31] reviewed three independent meta-analysis studies: The European Group Study of High Blood Pressure in the Elderly (n=840), The European Study of Systolic Hypertension (n=4695) and The Systolic Hypertension Study in the Chinese Population (n=2394).[31] The results of these meta-analyses revealed that a 10 mmHg increase in pulse pressure led to a 13% increase in all coronary events and a 20% increase in cardiovascular mortality. In the Framingham study population (middle and advanced age groups) investigated by Franklin et al.[32] SBP and pulse pressure were found to be positively associated with cardiovascular mortality and negatively correlated with diastolic blood pressure.[32] In addition, for the same age groups, the study found that cardiovascular mortality decreased in patients with high DBP values. However, pulse pressures were similar according to MS-Score, which may be due to the fact that MS-Score are mostly used for diabetes mellitus prediction or that MS-Score contain different epigenetic type, there are gaps in this field and need to be clarified with controlled studies.

Another finding of our study is that the RDP is more common in patients with MS-ATP III than in those without. Yan et al.[33] found that; MS was associated with RDP in men (but not women). In another study, Yan et al.[34] revealed that lacunar infarct and RDP are related. Chen et al.[35] observed that small vessel disease is associated with RDP frequency in patients with HT. Kim et al.[36] found that the RDP is associated with mortality. Cuspidi et al.[37] in a meta-analysis investigating the RDP and subclinical cardiac organ damage, found that the left ventricular mass index is higher in the RDP than in the DP and NDP. On the other hand, the frequency of RDP was similar between those with high MS-Score and those with low MS-Score. Again, it is not easy to explain the reason for this situation. The higher frequency of RDP in MS-ATP III patients may be a coincidental finding due to the small sample size and this effect may disappear as the sample size increases. Alternatively, the frequency of RDP may be higher in MS-ATP III and there may be no difference in RDP between high MS-Score and low MS-Score, reflecting different epigenetic types of MS.

Our study has some weaknesses. First, one weakness of our study may stem from the small sample size of the patients; therefore, we may not have been able to detect some relationships. Another weakness is that we did not investigate end organ damage. Finally, the fact that power analysis was not performed while designing the study may have caused some relationships not to be detected. MS is a cluster of risk factors for atherosclerotic diseases. However, patients with MS seem to have a higher atherosclerotic risk than the risks posed by these factors separately; larger prospective studies are needed to reveal this.

CONCLUSION

On one hand, the NDP frequency does not show a different distribution in patients with MS in both diagnostic methods; on the other hand, the RDP is found to be higher in patients with MS ATP III, but not in high MS-Score. As a result, no effect of MS on blood pressure changes during the day was detected.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of the İstanbul No:1 Clinical Researches Ethics Committee (Date: 10.11.2009, Decision No: B-007).

Informed Consent: Informed consent was obtained from all individual participants included in the 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 of 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.

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