Original Paper

Clinical Correlates of Ambulatory Blood Pressure Phenotypes at a Tertiary Care Hospital in Turkey

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Key Words

Ambulatory blood pressure monitoring • Cardiovascular risk • Hypertension • Masked hypertensive • Sustained hypertensive • Sustained normotensive • White coat hypertensive

Abstract

Background/Aims: Hypertension and its complications are major public health issues worldwide due to their association with high cardiovascular morbidity and mortality. Despite significant progress in health, the prevalence of hypertension is increasing. Ambulatory blood pressure monitoring (ABPM) is becoming increasingly important for the management of hypertension. In this study, we aimed to investigate the clinical and laboratory correlates of ambulatory blood pressure (ABP) phenotypes at a tertiary care hospital in Turkey. **Methods:** The characteristics of 1053 patients were retrospectively obtained from the hospital database. Hypertension was defined as patients with office blood pressure (BP) $\geq 140/90$ mmHg and/or previously diagnosed hypertension and/or the use of antihypertensive medication. According to the office BP and ABPM results patients were identified namely: (1) sustained normotensive (SNT) patients (both office BP and ABPM were normal), (2) sustained hypertensive (SHT) patients (both office BP and ABPM were high), (3) masked hypertensive (MHT) patients (office BP were normal, but ABPM were high), (4) white coat hypertensive (WCHT) patients (office BP were above limits, but ABPM were normal). **Results:** A total of 1053 patients were included to the study (female/male: 608/445 and mean age 55 ± 15 years). The mean age of patients with hypertension was significantly higher than without hypertension ($p < 0.0001$). Hypertension was more frequent in females ($p = 0.009$). The rates of history of diabetes mellitus (DM), hyperlipidemia (HL), and chronic kidney disease (CKD) were higher in patients with hypertension ($p < 0.0001$). Among patients with hypertension ($n = 853$, 81%), ABPM results showed that 388 (45%) of patients had SHT, 92 (11%) had MHT, and 144 (17%) had WCHT, whereas 229 (27%) had SNT. Patients with MHT were significantly older than patients with SNT ($p = 0.025$). The prevalence of SHT was higher in men than in women, whereas the prevalence

of WCHT was higher in women than in men ($p < 0.0001$). There was no significant difference between 4 groups with regard to body mass index ($p = 0.142$), a history of DM ($p = 0.189$) and smoking status (self-reported) ($p = 0.306$). Patients with SHT had the highest prevalence of history of hypertension, HL and CKD ($p < 0.0001$). Among patients without hypertension, 26 (13%) of patients had MHT and none of those patients was on antihypertensive treatment.

Conclusion: Potential usages of ABPM in Turkey may include screening of high risk individuals who have traditional cardiovascular risk factors. It also provides clinicians valuable information on abnormal ABP phenotypes. Future studies are needed to clarify the risk factors of different ABP phenotypes and to evaluate the role of ABPM on detection and control of hypertension.

Introduction

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Hypertension is an important public health issue worldwide. The prevalence of hypertension is increasing and it is predicted to reach 1.56 billion adults in 2025. However, hypertension is also frequently preventable risk factor of stroke, cardiovascular and kidney disease [1]. High blood pressure is the leading single risk factor for global disease burden and annually 9.4 million deaths have been attributed to effects of hypertension [2]. In 2003, the data collected from the prevalence, awareness, treatment and control of hypertension in Turkey (Patent) study showed that the prevalence of hypertension among Turkish adult population was 31.8% [3]. Subsequently, there was no significant change the prevalence of hypertension at Patent 2 study conducted in 2012, but the rates of awareness, treatment, and control of hypertension partially improved in our country [4]. Accurate measurement of the blood pressure (BP) is very important in the diagnosis and effective management of hypertension. Compared with conventional BP measurements, ambulatory blood pressure monitoring (ABPM) provides an insight individual BP phenotypes and it is more closely related to target organ damage and cardiovascular risk [5, 6]. In this study, we aimed to investigate the clinical and laboratory correlates of ambulatory blood pressure (ABP) phenotypes at a tertiary care hospital in Turkey.

Materials and Methods

Study population

The study was conducted in accordance with Declaration of Helsinki and approved by Ankara University School of Medicine Ethical Committee for Clinical Studies. Patients who were older than 18 years and had adequate 24-hour (24-h) ABPM recordings (at least 70% of measurements were satisfactory) were included in the study. Patients with known end-stage kidney disease requiring dialysis (48 patients) and inadequate 24-h ABPM recordings (57 patients) were excluded.

Data collection

Data were retrospectively analyzed from 1053 patients who had 24-h ABPM at Ankara University School of Medicine, Department of Nephrology, Hypertension Laboratory between January 2012-December 2016. The clinical characteristics and laboratory results of all patients were obtained from the hospital database. Clinical features including age, gender, height, weight, body mass index (BMI), smoking status, salt intake, office BP measurements, use of antihypertensive medication and comorbid conditions, were recorded. For laboratory values, serum creatinine and estimated glomerular filtration rate (eGFR) were determined. The eGFR was calculated using a 4 variable modification of diet in renal disease [7].

Antihypertensive drugs were classified as angiotensin-converting enzyme inhibitors (ACEi), angiotensin receptor blockers (ARBs), calcium channel blockers (CCBs), central acting agents (CAAs), α -blockers, β -blockers and diuretics. The single-pill combinations were comprised ACEi + diuretics, ARBs + diuretics, ACEi + CCBs and ARBs + CCBs.

BP measurements and definitions

All patients had office BP measurements and 24-h ABPM. Office BP measurements were taken using after 5 min of rest in a sitting position, using an oscillometric automatic sphygmomanometers, with a suitably sized cuff based on the circumference of the upper arm. Before the BP measurements, none of the patients had alcohol consumption, cigarette smoking, coffee or tea intake and exercise for at least 30 min. If the reading was higher in one arm, that arm was used for the following measurements. At least three consecutive BP measurements were obtained, with a time interval of at least 5 min between each measurement according to the recommendations of the European Society of Hypertension. If the difference between last two measurements was less than 5 mmHg, the arithmetic mean of the second and third BP measurements was noted as the office BP [8].

The 24-h ABPM was performed using a Spacelabs 90207 device (Spacelabs Inc., Redmond, Washington, USA). Patients were informed about the device and the procedure. They were told to maintain normal daily activities but to avoid from heavy exercise and to stay immobile at the time of cuff inflation. The patients were asked to provide information about diaries, including awake and sleep time, the times of drug ingestion and meals. Measurements were made between 07:00 and 23:00 (daytime) at 30 min intervals and between 23:00 and 07:00 (nighttime) every at 30 min intervals. Thus, the average systolic and diastolic BP, heart rate and mean BP were obtained for 24-h day and nighttime.

Hypertension was defined as an average office systolic blood pressure (SBP) of at least 140 mmHg, average office diastolic blood pressure (DBP) of at least 90 mmHg and/or previously diagnosed hypertension and/or the use of antihypertensive medication. According to the 24-h ABPM and office BP results patients were separated into 4 groups: (*Group 1*) *sustained normotensive (SNT) patients* (office SBP/DBP <140/90 mmHg and 24-h average SBP/DBP <130/80 mmHg and daytime average SBP/DBP <135/85 mmHg and nighttime average SBP/DBP <120/70 mmHg), (*Group 2*) *sustained hypertensive (SHT) patients* (office SBP ≥140 mmHg and/or DBP ≥90 mmHg and 24-h average SBP ≥130 mmHg and/or DBP ≥80 mmHg and/or daytime average SBP ≥135 mmHg and/or DBP ≥85 mmHg and/or nighttime average SBP ≥120 mmHg and/or DBP ≥70 mmHg), (*Group 3*) *masked hypertensive (MHT) patients* (office SBP/DBP <140/90 mmHg and 24-h average SBP ≥130 mmHg and/or DBP ≥80 mmHg and/or daytime average SBP ≥135 mmHg and/or DBP ≥85 mmHg and/or nighttime average SBP ≥120 mmHg and/or DBP ≥70 mmHg), (*Group 4*) *white coat hypertensive (WCHT) patients* (office SBP/DBP ≥140/90 mmHg and 24-h average SBP/DBP <130/80 mmHg and daytime average SBP/DBP <135/85 mmHg and nighttime SBP/DBP <120/70 mmHg [9].

Compared with daytime BP values, more than 10% decline in BP during the night was defined as dipper and at least less than 10% decline in BP during the night was defined as nondipper. Reverse dipper was defined nighttime BP values higher than daytime BP values [9].

Statistical analysis

SPSS 16.0 version (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. All values are shown as mean ± standard deviation or as a case number. Demographic parameters differences between two groups were analyzed using 2-sample t test or Mann-Whitney U test. Parameters differences among 4 groups were examined using an ANOVA variance analysis test. For post hoc analysis of non-normally distributed variables, Bonferroni corrected Mann-Whitney U test was used. Categorical variables were evaluated using Pearson's chi-square or Fischer exact tests. Results were considered statistically significant for P<0.05.

Results

Characteristics of patients

The characteristics of the study population (n=1053) are given in Table 1. Requests for ABPM were made from outpatient clinics of nephrology (n=590, 56%), neurology (n=254, 24.1%), internal medicine (n=81, 7.7%), geriatrics (n=34, 3.2%), endocrinology (n=28, 2.7%) and cardiology (n=66, 6.3%). They were 608 (58%) women and 445 (42%) men. The mean age was 55 ± 15 years (range, 18-90 years) and mean BMI was 28 ± 5 kg/m². The rates of history of hypertension, diabetes mellitus (DM), hyperlipidemia (HL) and chronic kidney disease (CKD) among the entire patients were 66.7, 19.2, 30 and 23%, respectively.

More than half of the patients were using antihypertensive medication. A total of 449 (43%) patients were dipper, 444 (42%) were nondipper, and 160 (15%) were reverse dipper. The mean office SBP was 140 ± 20 mmHg and mean office DBP was 87 ± 25 mmHg. The mean 24-h SBP was 127 ± 16 mmHg and mean 24-h DBP was 78 ± 24 mmHg. The mean eGFR of the study participants was 83 ± 33 ml/min/1.73m² (MDRD-4).

Comparison of patients with and without hypertension

The comparison of patients with and without hypertension is shown in Table 2. According to definition of hypertension (patients with office BP $\geq 140/90$ mmHg and/or previously diagnosed hypertension and/or the use of antihypertensive medication), 853 (81%) of all participants were identified as hypertensive. The mean age of hypertensive patients was significantly higher than non-hypertensive patients (56 ± 15

vs. 49 ± 15 , $p < 0.0001$). Hypertension was more common among females ($p = 0.009$). The rates of history of HL, DM and CKD among hypertensive patients were significantly higher than those among non-hypertensive patients (33.6% vs. 14.2%, 21.9% vs. 7.6%, 30% vs. 3.5%, respectively, $p < 0.0001$). There was no difference between two groups with respect to active smoking status (self-reported) and BMI (11.2% vs. 16.2%, 28 ± 5 vs. 28 ± 5 , respectively, $p > 0.05$). In patients with hypertension, the mean office SBP and DBP were significantly higher than those without hypertension (144 ± 20 mmHg vs. 123 ± 12 mmHg, 89 ± 28 mmHg vs. 79 ± 9 mmHg, respectively, $p < 0.0001$).

ABP phenotypes of patients with or without hypertension

Among patients with hypertension, ABPM results showed that 388 (45%) patients had SHT, 92 (11%) had MHT, and 144 (17%) had WCHT, whereas 229 (27%) had SNT. Among patients without hypertension, 26 (13%) of patients had MHT and none of those patients was on antihypertensive treatment. There was no difference in terms of MHT among hypertensive and non-hypertensive patients (11% vs. 13%, $p > 0.05$). The rate of reverse dipper was higher among hypertensive patients compared with non-hypertensive (17% vs. 8%, $p = 0.002$) (Table 2).

Among patients with hypertension, 70% of those patients were taking antihypertensive treatment and only 27% of them had BP under control. The majority has been receiving with one or more drugs (one drug: 23.4% vs. 2 drugs: 22.8% vs. 3 or more drugs: 22.1%). The percentages of patients taking antihypertensive drugs were ACEi (20.6%), ARBs (36.8%), CCBs (38.2%), α -blockers (18%), β -blockers (32.5%), CAAs (0.5%) and diuretics (30%). The

Table 1. The characteristics of the study population. Abbreviations: SD, standard deviation; BMI, body mass index; HT, hypertension; HL, hyperlipidemia; DM, diabetes mellitus; CKD, chronic kidney disease; SBP, systolic blood pressure; DBP, diastolic blood pressure; ABPM, ambulatory blood pressure monitoring; eGFR, estimated glomerular filtration rate; MDRD, modification of diet in renal disease. All values are shown as mean $\pm$ standard deviation or as a case number

Patient's characteristics	Results
Age (years) (mean $\pm$ SD)	55 $\pm$ 15
Gender (n, male/female)	445/608
BMI (kg/m ²) (mean $\pm$ SD)	28 $\pm$ 5
History of HT (n,+/-)	702/351
History of HL (n,+/-)	304/710
History of DM (n,+/-)	200/841
History of CKD (n,+/-/renal transplantation)	240/774/12
Salt restricted diet (self-reported) (n,+/-)	361/612
Smoking status (self-reported) (n,+/-)	117/844
Antihypertensive medication (n,+/-)	588/465
Dipper/Nondipper/Reverse dipper	449/444/160
Office SBP (mmHg) (mean $\pm$ SD)	140 $\pm$ 20
Office DBP (mmHg) (mean $\pm$ SD)	87 $\pm$ 25
Average 24-h ABPM SBP (mmHg) (mean $\pm$ SD)	127 $\pm$ 16
Average 24-h ABPM DBP (mmHg) (mean $\pm$ SD)	78 $\pm$ 24
Average 24-h ABPM daytime SBP (mmHg) (mean $\pm$ SD)	130 $\pm$ 16
Average 24-h ABPM daytime DBP (mmHg) (mean $\pm$ SD)	79 $\pm$ 11
Average 24-h ABPM nighttime SBP (mmHg) (mean $\pm$ SD)	121 $\pm$ 17
Average 24-h ABPM nighttime DBP (mmHg) (mean $\pm$ SD)	72 $\pm$ 11
eGFR (MDRD) (ml/min/1.73m ²) (mean $\pm$ SD)	83 $\pm$ 33

Table 2. Comparison of characteristics of hypertensive and non-hypertensive patients. Abbreviations: SD, standard deviation; BMI, body mass index; HL, hyperlipidemia; DM, diabetes mellitus; CKD, chronic kidney disease; SBP, systolic blood pressure; DBP, diastolic blood pressure; BP, blood pressure; ABPM, ambulatory blood pressure monitoring; ACEi, angiotensin-converting enzyme inhibitors; ARBs, angiotensin receptor blockers; CCBs, calcium channel blockers; CAAs, central acting agents; eGFR, estimated glomerular filtration rate; MDRD, modification of diet in renal disease. All values are shown as mean $\pm$ standard deviation or as a case number or percentage. *p-value is based on 2-sample t test. **p-value is based on Pearson's chi-square or Fischer exact tests

Parameters	Hypertension (+) n:853 (%81)	Hypertension (-) n:200 (%19)	P value
Age (years) (mean $\pm$ SD)	56 $\pm$ 15	49 $\pm$ 15	<0.0001*
Gender (n, %) (male/female)	377/476 (44%/56%)	68/132 (34%/66%)	0.009**
BMI (kg/m ²) (mean $\pm$ SD)	28 $\pm$ 5	28 $\pm$ 5	>0.05*
History of HL (n,+) (%)	277 (33.6%)	27 (14.2%)	<0.0001**
History of DM (n,+) (%)	185 (22%)	15 (7.6%)	<0.0001**
History of CKD (n,+) (%)	233 (27.6%)	7 (3.5%)	<0.0001**
Salt restricted diet (self-reported) (n,+) (%)	341 (43.7%)	20 (10.4%)	<0.0001**
Smoking status (self-reported) (n,+) (%)	86 (11.2%)	31 (16.2%)	>0.05**
Office SBP (mmHg) (mean $\pm$ SD)	144 $\pm$ 20	123 $\pm$ 12	<0.0001*
Office DBP (mmHg) (mean $\pm$ SD)	89 $\pm$ 28	79 $\pm$ 9	<0.0001*
ABPM results (n, %)			
• Sustained normotensive	229 (27%)	165 (82%)	<0.0001**
• Sustained hypertensive	388 (45%)	6 (3%)	<0.0001**
• Masked hypertensive	92 (11%)	26 (13%)	>0.05**
• White-coat hypertensive	144 (17%)	3 (2%)	<0.0001**
Status of nocturnal fall of BP			
• Dipper (n, %)	359 (42%)	90 (45%)	>0.05**
• Nondipper (n, %)	350 (41%)	94 (47%)	>0.05**
• Reverse dipper (n, %)	144 (17%)	16 (8%)	0.002**
Antihypertensive medication (n, %)			
• ACEi	153 (20.6%)		
• ARBs	273 (36.8%)		
• CCBs	283 (38.2%)		
• Diuretics	223 (30%)		
• β -blockers	240 (32.4%)		
• α -blockers	134 (18%)		
• CAAs	4 (0.5%)		
• Single-pill combination	228 (30.8%)		
eGFR (MDRD) (ml/min/1.73m ²) (mean $\pm$ SD)	79 $\pm$ 33	102 $\pm$ 26	<0.0001*

rate of patients using single-pill combination was 30.8%. The most frequently prescribed single-pill combination was ARBs + diuretics (21.6%). The mean eGFR among hypertensive patients was less than those among non-hypertensive patients (79 $\pm$ 33 ml/min/1.73m² vs. 102 $\pm$ 26 ml/min/1.73m², p<0.0001) (Table 2).

Differences in clinical and laboratory parameters among four groups of ABP phenotypes

According to office BP and ABPM results, patients were divided into 4 groups as listed below: Group 1 (n=394, 37.5%) was composed of patients with SNT;

Group 2 (n=394, 37.5%) was composed of patients with SHT;

Group 3 (n=118, 11%) was composed of patients with MHT;

Group 4 (n=147, 14%) was composed of patients with WCHT.

The comparative clinical and laboratory parameters of groups are given in Table 3. Patients with MHT were significantly older compared to patients with SNT (58 $\pm$ 15 vs. 53 $\pm$ 15, p=0.025). The prevalence of SHT was higher in men than women, whereas the prevalence of WCHT was higher in women than men (p<0.0001). There was no significant difference between 4 groups with regard to BMI (p=0.142), a history of DM (p=0.189) and smoking status (self-reported) (p=0.306). Patients with SHT had the highest prevalence of history of hypertension, HL and CKD (p<0.0001). Also, the use of antihypertensive medication and implementation of salt-restricted diet were statistically higher in patients with SHT (p<0.0001). eGFR levels were not different among the groups (p>0.05). In patients receiving

antihypertensive medication, the rates of MHT and WCHT patients were 12.8% and 13.6%, respectively. The rate of hypertension control was 31.3%.

Comparison of office BP and ABPM results among four groups

Comparison of office BP and ABPM results among patients with SNT, SHT, MHT, and WCHT are presented in Table 3. In patients with MHT, office SBP was significantly lower than SHT patients and WCHT patients (128 ± 10.5 mmHg vs. 157 ± 16 mmHg vs. 151 ± 13.5 mmHg, $p < 0.0001$), but it was significantly higher than SNT patients (128 ± 10.5 mmHg vs. 124 ± 13 mmHg, $p = 0.029$). The office DBP of MHT patients was also significantly lower than SHT patients and WCHT patients (81 ± 9 mmHg vs. 97 ± 38 mmHg vs. 92 ± 9 mmHg, $p < 0.0001$), while there was no significant difference between MHT and SNT patients (81 ± 9 mmHg vs. 78 ± 9 mmHg, $p > 0.05$). Average ambulatory 24-h, daytime and nighttime SBP levels were different among 4 groups of patients ($p < 0.0001$). Average ambulatory 24-h, daytime and nighttime DBP levels were not different in patients with SNT and WCHT ($p > 0.05$). Also, average ambulatory 24-h and nighttime DBP levels were not different between SHT and MHT patients ($p > 0.05$).

Characteristics of nocturnal BP change

Comparison of fall of nocturnal BP among patients with SNT, SHT, MHT, and WCHT showed that dipper, nondipper and reverse dipper were significant differences among groups (Table 4). Prevalence of reverse dipper pattern was significantly higher in patients with SHT than other groups ($p < 0.0001$).

Table 3. Clinical and laboratory parameters among four groups of patients according to ABP phenotypes. Abbreviations: SD, standard deviation; BMI, body mass index; eGFR, estimated glomerular filtration rate; MDRD, modification of diet in renal disease; HT, hypertension; HL, hyperlipidemia; DM, diabetes mellitus; CKD, chronic kidney disease; SBP, systolic blood pressure; DBP, diastolic blood pressure; ABP, ambulatory blood pressure; ABPM, ambulatory blood pressure monitoring. All values are shown as mean $\pm$ standard deviation or as a case number. *p-value is based on one way ANOVA test. **p-value is based on Pearson's chi-square or Fischer exact tests. Groups with significant differences according to the Benferroni corrected Mann-Whitney U-test are depicted in superscript roman

Parameters	Group I (SNT patients) (n=394)	Group II (SHT patients) (n=394)	Group III (MHT patients) (n=118)	Group IV (WCHT patients) (n=147)	P value
Age (years) (mean $\pm$ SD)	53 $\pm$ 15 ^{III}	56 $\pm$ 15	58 $\pm$ 15 ^I	55 $\pm$ 17	0.017*
Gender (n, male/female)	129/265 ^{II,III}	206/188 ^I	59/59 ^{IV}	51/96 ^{III}	<0.0001**
BMI (kg/m ²) (mean $\pm$ SD)	28 $\pm$ 5	28 $\pm$ 5	26 $\pm$ 5	29 $\pm$ 5	>0.05*
History of HT (n,+/-)	221/173 ^{II,III}	294/100 ^I	91/27 ^{IV}	96/51 ^{III}	<0.0001**
History of HL (n,+/-)	86/291 ^{III,IV}	115/268	38/79 ^{IV}	65/72 ^{III}	<0.0001**
History of DM (n,+/-)	62/328	81/308	24/94	33/111	>0.05**
History of CKD (n,+/-/renal transplantation)	62/321/4 ^{III,III}	114/257/10 ^I	36/80/2 ^I	28/116/1	<0.0001**
Salt restricted diet (self-reported) (n,+/-)	110/264 ^{II,III}	150/219 ^I	55/56 ^I	46/73	<0.0001**
Smoking status (self-reported) (n,+/-)	41/328	53/310	10/102	13/104	>0.05**
Antihypertensive medication (n,+/-)	184/210 ^{II,III}	249/145 ^I	75/43 ^I	80/67	<0.0001**
Office SBP (mmHg) (mean $\pm$ SD)	124 $\pm$ 13 ^{II,III,IV}	157 $\pm$ 16 ^{III,IV}	128 $\pm$ 10.5 ^{II,IV}	151 $\pm$ 13.5 ^{I,III}	<0.0001*
Office DBP (mmHg) (mean $\pm$ SD)	78 $\pm$ 9 ^{II,IV}	97 $\pm$ 38 ^{III}	81 $\pm$ 9 ^{II,IV}	92 $\pm$ 9 ^{III}	<0.0001*
Average 24-h ABPM SBP (mmHg) (mean $\pm$ SD)	114 $\pm$ 8 ^{II,III,IV}	142 $\pm$ 12 ^{III,IV}	132 $\pm$ 9 ^{II,IV}	120 $\pm$ 7 ^{II,III}	<0.0001*
Average 24-h ABPM DBP (mmHg) (mean $\pm$ SD)	72 $\pm$ 37 ^{II,III}	84 $\pm$ 10 ^{IV}	81 $\pm$ 7 ^{IV}	72 $\pm$ 6 ^{II,III}	<0.0001*
Average 24-h ABPM daytime SBP (mmHg) (mean $\pm$ SD)	118 $\pm$ 9 ^{II,III,IV}	145 $\pm$ 12 ^{III,IV}	133 $\pm$ 9 ^{II,IV}	123 $\pm$ 8 ^{II,III}	<0.0001*
Average 24-h ABPM daytime DBP (mmHg) (mean $\pm$ SD)	73 $\pm$ 6 ^{II,III}	87 $\pm$ 11 ^{II,III,IV}	83 $\pm$ 8 ^{II,IV}	74 $\pm$ 7 ^{II,III}	<0.0001*
Average 24-h ABPM nighttime SBP (mmHg) (mean $\pm$ SD)	108 $\pm$ 9 ^{II,III,IV}	135 $\pm$ 15 ^{III,IV}	128 $\pm$ 13 ^{II,IV}	114 $\pm$ 11 ^{I,II,III}	<0.0001*
Average 24-h ABPM nighttime DBP (mmHg) (mean $\pm$ SD)	65 $\pm$ 6 ^{II,III}	79 $\pm$ 11 ^{IV}	77 $\pm$ 8 ^{IV}	67 $\pm$ 8 ^{II,III}	<0.0001*
eGFR (MDRD) (ml/min/1.73m ²)	87.5 $\pm$ 31	78 $\pm$ 34	84 $\pm$ 37	84 $\pm$ 35	>0.05*

Table 4. Characteristics of nocturnal BP change among four groups. Abbreviations: BP, blood pressure; SNT, sustained normotensive; SHT, sustained hypertensive; MHT, masked hypertensive; WCHT, white-coat hypertensive. All values are shown as a case number or percentage. *p-value is based on Pearson's chi-square or Fischer exact tests. Groups with significant differences according to the Benferroni corrected Mann-Whitney U-test are depicted in superscript roman

Status of nocturnal BP change	Group I (SNT patients) (n:394)	Group II (SHT patients) (n:394)	Group III (MHT patients) (n:118)	Group IV (WCHT patients) (n:147)	P value
Dipper (n, %)	182 (40.5%) ^{III,IV}	168 (37.5%) ^{III,IV}	32 (7%) ^{I,II}	67 (15%) ^{I,II}	<0.0001*
Nondipper (n, %)	173 (39%) ^{III,IV}	164 (37%) ^{III,IV}	48 (11%) ^{I,II}	59 (13%) ^{I,II}	<0.0001*
Reverse dipper (n, %)	39 (24%) ^{II}	62 (39%) ^{I,III,IV}	38 (24%) ^{II}	21 (13%) ^{II}	<0.0001*

Discussion

In the current study, a total of 851 study participants (81%) were hypertensive and the prevalence of hypertension was more common among females ($p=0.009$). The mean age of hypertensive patients was higher than non-hypertensive ($p<0.0001$). The presence of traditional cardiovascular risk factors such as HL, DM, CKD was higher in patients with hypertension ($p<0.0001$), but no remarkable difference was observed in terms of the smoking status (self-reported) and BMI among patients with hypertension and without ($p>0.05$). According to the ABPM results in patients with hypertension, our study showed that 11% of patients had MHT, 17% had WCHT, and 45% had SHT, while 27% had well controlled BP. We also found that patients with hypertension had the high rate of reverse dipper pattern compared to patients without hypertension (17% vs 8%, $p=0.002$). We also found that the prevalence of MHT patients was 11%, whereas that of WCHT patients was 14%. We observed that patients with MHT was older than other three groups and it was significant only compared to SNT patients ($p=0.025$). We also found that SHT was more common in men, whereas WCHT in women ($p<0.0001$). Our data showed that there was no significant difference in eGFR among patients with SNT, SHT, MHT and WCHT. Nocturnal BP patterns (dipper, nondipper and reverse dipper) were significantly different among four groups. Particularly, reverse dipper pattern was high in patients with SHT.

ABPM is becoming increasingly important for evaluation of hypertension. Compared with office BP measurement, ABPM provides more accurate assessment of BP and prediction of cardiovascular outcomes [10]. The growing use of ABPM has led to identification of abnormal ABP phenotypes and high BP variability. Thus, it allows the recognition of individual risk profile of patients. It can be helpful in identifying patients at increased risk of developing sustained hypertension and cardiovascular events [11]. Also, elevated BP variability during ABPM is associated with increased risk of cardiovascular events, cerebral and renal damage [12, 13].

However, the clinical relevance of WCHT and MHT is debatable. In a meta-analysis conducted in 2011 about the prognostic significance of WCHT and MHT diagnosed by ABPM, showed that the cardiovascular risk was not significantly different between WCHT and normotensive patients. In the same study, compared to normotensive patients, MHT, WCHT and SHT were associated with increased risk for adverse clinical outcomes [14]. In other studies, Cuspidi et al. [15] and Tadic et al. [16] demonstrated the harmful effects of white coat on heart in patients with WCHT. In another meta-analysis performed by Briasoulis et al., WCHT was associated with higher rates of cardiovascular morbidity and mortality compared with normotensive patients, but not significantly different in all-cause mortality and stroke risk [17].

The prevalence of WCHT and MHT are varying based on patient characteristics and study population. Risk factors related to WCHT are age, female sex and non-smoking status. Male sex, relatively younger age, being smoker, alcohol consumption, stress, increased physical activity, high salt intake and the presence of diabetes, obesity and kidney disease were found to be associated with MHT [18-20]. Therefore, the identification of WCHT and

MHT patients via ABPM is important in patients with high cardiovascular risk profiles to provide a proper management of those patients. In our study population, we did not evaluate target organ damage. Based on ABP phenotypes, among patients with SNT, SHT, MHT and WCHT, we did not find significant differences in smoking status, presence of diabetes, eGFR and BMI. We found that patients with MHT were older and WCHT was more common in women. Our results showed that the rates of MHT and WCHT patients in diabetics were 12% and 16.5%, respectively. In patients with CKD the prevalence of MHT was 15%, while that of WCHT was 11%. In addition to clinical determinants of cardiovascular risk factors, ABPM provides a comprehensive assessment of BP profile and adds prognostic information on the development of cardiovascular events in high-risk hypertensive patients. Hence, in high risk individuals ABPM should be kept in mind [21].

Several studies examining the relationship between circadian BP patterns and cardiovascular risk, were shown not only an increase target organ damage and cardiovascular events, but also predictor of cardiovascular risk in both hypertensive and normotensive patients [22-24]. In the present study, among patients with hypertension, nondipper BP pattern was found in 350 (41%) patients. In addition, among patients without hypertension, 94 (47%) had nondipper. Also we found that the rate of reverse dipper pattern was significantly higher in patients with hypertension than those without hypertension. We also found that there were significant differences with regard to different nocturnal BP patterns (dipper, nondipper and reverse dipper) among patients with various ABP phenotypes (SNT, SHT, MHT and WCHT). The use of ABPM provides information on circadian BP pattern and it may also predict prognosis related to target organ damage and cardiovascular outcomes.

In the last years, current guidelines have defined the use of ABPM for the management of hypertension in clinical practice. In 2013, the European Society of Hypertension (ESH) / European Society of Cardiology (ESC) guidelines recommended both ABPM and home BP measurement as an adjunct to office BP measurement [8]. In addition, in the 2013 ESH/ESC guideline, specific indications for ABPM were as follows: (i) marked discordance between office BP and home BP; (ii) assessment of dipping status; (iii) suspicion of nocturnal hypertension or absence of dipping, such as in patients with sleep apnea, CKD, or DM; (iv) assessment of BP variability. The ESH Working Group on Blood Pressure Monitoring and Cardiovascular Variability published a new consensus document for ABPM in 2014, and presented an up to date summary of the clinical indications for the use of ABPM in daily practice [9]. The National Institute for Health and Care Excellence (NICE) guidelines recommended the use of ABPM to confirm diagnosis of hypertension if the clinic BP of 140/90 mmHg or higher [25]. In contrast, the guidelines of the American Eighth Joint National Committee (JNC 8) did not mention on ABPM [26]. The National Heart Foundation of Australia's Guideline for the diagnosis and management of hypertension in adults recommended that ABPM and/or home BP monitoring, if clinic BP is $\geq 140/90$ mmHg or hypertension is suspected [27]. The Hypertension Canada's 2017 Guidelines recommends that the out-of-office BP assessment should preferably be done by ABPM, if the office BP readings are elevated [28].

In Turkey, the Turkish Hypertension Consensus Report has been published in 2015 in order to create a standardized approach to diagnosis and treatment of hypertension in adults. In this report, it has been suggested that if the clinic BP is $\geq 140/90$ mmHg, the diagnosis of hypertension must be confirmed by repeated clinical BP measurements and/or whenever possible by ABPM or home BP measurements [29]. However, according to the results of a recent nationwide field survey in Turkey, the prevalence of ownership of a home sphygmomanometer among hypertensive subjects was found as 20.1 %, and the usage of wrist devices and non-validated devices were common [30]. Home BP monitoring is not a viable option until the implementation of a hypertension care program consisting of reimbursement of a validated sphygmomanometer in Turkey.

Although the above consensus report emphasizes the importance of ABPM for the management of patients with hypertension, ABPM cannot be also adequately implemented in clinical practice due to limited availability of ABPM devices in many clinical settings in

Turkey. Numerous researches over past three decades have established ABPM as an evidence-based and cost-effective gold-standard for the diagnosis and treatment of hypertension. But, if the resources and its availability are limited, ABPM is recommended only marked discordance between clinical BP and home BP, assessment of dipping status, suspicion of nocturnal hypertension and assessment of BP variability [29]. Potential usages for ABPM in our country may include screening of individuals who have traditional cardiovascular risk factors. Use of ABPM can reduce misdiagnosis, and unnecessary treatment, and lead to better control of BP. Clinicians should use ABPM whenever possible and take initiatives to establish ABPM services where those do not exist. However, if ABPM is to be widely used in general practice, there is a need to establish appropriate educational activities and to improve the methods of presenting and analyzing ABPM results in a national program for hypertension.

This study has some limitations. The major limitations of our study were its retrospective design and partially based on self-reported data on comorbidities. Other limitation of the study was that the patients were diagnosed abnormal ABP phenotypes based on a single ABPM. Another limitation of the study was the lack of data on hypertensive end-organ damage, such as those for retinopathy, albuminuria, changes in the vasculature, and lack of echocardiography findings.

Conclusion

Potential usages for ABPM in Turkey may include screening of high risk individuals who have traditional cardiovascular risk factors. Future studies are needed to clarify the risk factors of different ABP phenotypes and to evaluate the role of ABPM on detection and control of hypertension. There is also a need for standardization protocol for indications of ABPM in low and middle income countries with limited availability of ABPM devices.

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Disclosure Statement

All authors declare that they have no conflicts of interest.

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