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Original research

PROFILES OF 24-HOUR AMBULATORY BLOOD PRESSURE MEASUREMENT AND THEIR ASSOCIATION WITH CARDIOVASCULAR RISK FACTORS IN ELDERLY HIGH-RISK HYPERTENSIVE PATIENTS

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ABSTRACT

Background: *Hypertension is prevalent in the elderly, affecting two-thirds of individuals aged 60 years and older. Ambulatory blood pressure measurement (ABPM) is recommended for diagnosing and managing hypertension in this population. This study aimed to characterize 24-hour ABPM profiles and their association with cardiovascular risk factors in older adults with high-risk hypertension.*

Methods: *A descriptive cross-sectional study included 96 patients aged ≥ 60 years, mean age 70.9 ± 7.9 years, 35.4% male (n = 34). Participants underwent routine clinical and laboratory assessments, including clinic and 24-hour ABPM. Pearson's correlation coefficient was used to analyze the relationships between BP profiles and risk factors (p < 0.05).*

Results: *Mean office systolic and diastolic blood pressure (BP) were 150.16 ± 26.06 mmHg and 81.46 ± 11.79 mmHg, respectively. Corresponding 24-hour ABPM values were 130.80 ± 17.43 mmHg and 73.73 ± 10.17 mmHg. The prevalence of masked uncontrolled hypertension was 12.5% (n = 12), morning surge was observed in 40.6% (n = 39), and 37.5% (n = 36) had isolated systolic hypertension. Nocturnal BP profiles were dipper [13.5% (n = 13), both systolic and diastolic], non-dipper [53.1%, (n = 51), systolic and/or diastolic], and riser [56.3% (n = 54), systolic and/or diastolic]. Mean 24-hour systolic BP correlated significantly with age (r = 0.229), body mass index (BMI) (r = 0.212), waist circumference (r = 0.226), creatinine level (r = 0.207), dyslipidemia (r = 0.223). Mean 24-hour diastolic BP significantly correlated with BMI (r = 0.294).*

Conclusion: *Elderly high-risk hypertensive patients demonstrated a higher incidence of isolated systolic hypertension, morning surge, and non-dipping patterns. Mean 24-hour systolic and diastolic were significantly associated with cardiovascular risk factors. These findings emphasize the importance of comprehensive 24-hour BP monitoring in this population for better management and risk assessment.*

Keywords: *High-risk hypertension, ambulatory blood pressure monitoring, cardiovascular risk factors, elderly population.*

I. INTRODUCTION

Hypertension is globally recognized as a significant risk factor for cardiovascular morbidity and mortality [1]. Its prevalence is notably high among the elderly population, affecting approximately two-thirds of individuals aged 65 years and older [2]. Ambulatory blood pressure measurement (ABPM) has emerged as the recommended method for diagnosing and managing hypertension, increasingly using 24-hour blood pressure (BP) monitoring for the elderly [3]. Epidemiological studies consistently demonstrate

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a progressive increase in the risk of cardiovascular disease, stroke, and renal disease as both systolic and diastolic BP levels rise [3-5]. Aging is associated with a notable elevation in systolic blood pressure (SBP) [6], often leading to the occurrence of isolated systolic hypertension (ISH) in the elderly population [7]. Previous research highlights the strong correlations between 24-hour ABPM and cardiovascular risk factors [8-10]. Understanding the conditions affecting the age-related increase in BP is of obvious clinical importance. In addition, effective control of cardiovascular risk factors plays a crucial role in mitigating the adverse impact of elevated BP on cardiovascular morbidity and mortality, particularly among elderly patients.

Despite the global evidence, there remains a scarcity of data regarding ABPM and its association with traditional cardiovascular risk factors in the elderly population in Vietnam. Therefore, our study aimed to address this gap by examining and characterizing 24-hour ABPM profiles and their relationship with cardiovascular risk factors in individuals aged 60 years and older with high-risk hypertension.

II. MATERIALS AND METHODS

2.1. Study design and participants

This cross-sectional single-center study included patients aged ≥ 60 years with a documented diagnosis of essential hypertension, regardless of office BP, under treatment with ≥ 1 antihypertensive drug stable for ≥ 1 months at the Department of Internal Medicine of the Becamex International Hospital (Binh Duong province, Vietnam) from June 2020 to June 2021. Hypertension diagnosis and management followed the guidelines of the Vietnamese Heart Association and the Vietnamese Society of Hypertension [11], which align with the current guideline [12]. Diagnosis of Hypertension was defined as SBP ≥ 140mmHg/or diastolic blood pressure (DBP) ≥ 90 mmHg on at least two separate measurements or a previously diagnosed and treated hypertension history [12].

High-risk hypertension patients included those with grade 1 hypertension with three or more risk factors or target organ damage, as well as individuals with stage 3 chronic kidney disease, diabetes mellitus, cardiovascular disease, or grade 2 hypertension coupled with one or more risk factors [12]. Exclusion criteria were those with secondary hypertension, individuals < 60 years old with hypertension, untreated hypertensive patients, those with acute illnesses or severe electrolyte disturbances, or participants with < 85% of total ABPM measurement time, and individuals who did not provide consent for the study.

2.2. Data collection

The study database recorded various clinical and demographic characteristics, medical history as well as laboratory, instrumental data. These included age, gender, weight, height, body mass index (BMI), duration of hypertension, known cardiovascular risk factors (eg, smoking habit, dyslipidemia, and diabetes mellitus), and clinical cardiovascular diseases. Laboratory evaluations included measurements of blood creatinine, fasting glucose, total cholesterol, low-density lipoprotein cholesterol (LDL-c), high-density lipoprotein cholesterol (HDL-c), and triglycerides. The echocardiographic studies were conducted in the morning following the recommendations of the American Society of Echocardiography [13]. Left ventricular hypertrophy (LVH) was defined as an left ventricular mass index (LVMI) exceeding 95 g/m² in women and 115 g/m² in men [17]. The left ventricular ejection fraction (LVEF) was estimated using the Simpson method.

2.3. Blood Pressure Measurements

Office BP was measured on the participant's left arm using the oscillometric device (Yamasu, wall type, Japan). Patients are required to rest in a quiet room for at least 5-10 minutes before BP measurement. They should avoid stimulants such as coffee, smoking, and alcohol for at least 2 hours prior to the measurement. BP should be measured twice, with an interval of at least 1-2 minutes between measurements. If the difference between the two measurements is greater than 10mmHg, additional measurements should be taken after a few minutes of rest. The recorded BP value is the average of the last two measurements. For individuals with rhythm disorders, such as atrial fibrillation, additional measurements may be taken.

24-hour ABPM was initiated immediately after recording the office BP. The measurements were performed using the Oscar2 device (SunTech Medical Inc, Morrisville, NC, USA), and the ABPM data was analyzed using the accompanying software package (AccuWinpro v3.4). BP recordings were taken every 30 minutes from 07:00 to 22:00 hours, and every 60 minutes from 22:00 to 07:00 hours, following the ABPM criteria outlined in the European Society of Hypertension guidelines [14]. Participants were given a diary to record the time they went to sleep at night and the time they woke up in the morning and were asked to avoid vigorous physical activities on the day of the test. A record was considered valid if it met the criteria of having ≥85% of valid measurement readings, excluding any abnormal or noisy measurements. Ambulatory BP readings of SBP < 70mmHg or > 260mmHg and/or DBP < 40mmHg or > 150mmHg were disregarded.

2.4. Definition of circadian patterns

The nocturnal BP decline and circadian patterns were determined by calculating the percentage of decline in both SBP and DBP during the night using the formula: (daytime BP - nighttime BP)/daytime BP [14]. A normal dipping pattern, referred to as a "dipper," was identified when the average SBP reduction during the night was greater than 10% of the mean SBP during the day. If this reduction exceeded 20%, the patient was classified as an "extreme dipper." An abnormal dipping pattern, known as a "non-dipper," was diagnosed when the average SBP reduction during the night was less than 10% compared to daytime values. The patient was classified as a "riser" when the mean nighttime SBP exceeded the daytime SBP [14]. The morning blood pressure surge (MBPS) is defined as an increase of at least 20/15 mm Hg between the morning SBP and DBP, which is calculated by comparing the average of the four 30-minute SBP and DBP readings taken during the first 2 hours after waking up with the lowest nighttime SBP and DBP. The lowest nighttime SBP and DBP are determined by averaging the three systolic and diastolic BP readings centered around the lowest nighttime reading [15].

The study adhered to the principles outlined in the Declaration of Helsinki and was independently approved by the local Ethics Committee of the Hue University of Medicine and Pharmacy (Approval No. H2020/346, June 18, 2020).

2.5. Statistical analysis

The data were analyzed using SPSS software, version 25. Continuous variables with a normal distribution were presented as mean ± standard deviation, while categorical variables were presented as absolute numbers (percentages): n (%). Non-normally distributed continuous variables were presented as median and values corresponding to the 25^{th} and 75^{th} percentiles. The Student's t-test was performed for continuous variables with a normal distribution, while the Mann-Whitney U test was used for non-normally distributed continuous variables. The chi-squared test or Fisher exact test was used for categorical variables. Pearson's correlation coefficient was employed to analyze the relationships between ABPM profiles and cardiovascular risk factor variables. All statistical tests performed in this study were two-sided, and statistical significance was determined when the p-value <0.05.

III. RESULTS

3.1. Patient Characteristics

The study included a total of 96 patients, mean age of 70.9 ± 7.9 years and 35.4% male (n=34). The baseline characteristics and laboratory finding of the studied patients were presented in Table 1 and Table 2.

Table 1: Demographic and clinical characteristic of studied participants

Variable	Total (n=96)
Age, years, M ± SD	70.9 ± 7.9
Duration of hypertension, n (%)	
< 1 year	15 (15.6)
1 - 5 years	42 (43.8)

Variable	Total (n=96)
6 - 10 years	21 (21.9)
> 10 years	18 (18.8)
Diabetes mellitus, n (%)	49 (51)
Smoking, n (%)	23 (24)
Dyslipidemia, n (%)	77 (80.2)
Family history of hypertension, n (%)	52 (54.2)
Low physical activity levels, n (%)	67 (69.8)
History of stroke, n (%)	11 (11.5)
BMI, kg/m^2, M ± SD	23.44 ± 3.29
Obesity status, n (%)	
Underweight	7 (7.3)
Normal weight	35 (36.5)
Overweight	26 (27.1)
Obesity	28 (29.2)
Waist circumference, cm, M ± SD	93.52 ± 12.25
Headache, n (%)	55 (57.3)
Dizziness, n (%)	61 (63.5)
Blurred vision, n (%)	41 (42.7)
Chest discomfort, n (%)	36 (37.5)
Clinic SBP, mm Hg, M ± SD	150.16 ± 26.06
Clinic DBP, mm Hg, M ± SD	81.46 ± 11.79

Abbreviation: *BMI: body mass index; DBP: systolic blood pressure; M: mean; SBP: systolic blood pressure; SD: standard deviation.*

Table 2: Laboratory and instrumental findings of studied participants

Variable	Total (n=96)
Creatinine, µmol/l, Me (IQR)	84.6 (90.4; 99)
Estimated GFR (mL/min/1.73 m^2), Me (IQR)	70.3 (56.7; 83.1)
Total Cholesterol, mmol/L, Me (IQR)	4.30 (3.62; 4.97)

Variable	Total (n=96)
HDL-c, mmol/L, Me (IQR)	0.85 (1.05; 1.26)
LDL-c, mmol/L, Me (IQR)	2.49 (1.76; 3.11)
Triglycerides, mmol/L, Me (IQR)	1.61 (1.22; 2.20)
Glucose, mmol/L, Me (IQR)	6.25 (5.30; 8.17)
Uric acid, mmol/L, Me (IQR)	334.95 (279.32; 435.72)
LVM, g, M ± SD	157,55 ± 52,72
LVMI, g/m^2, M ± SD	107.73 ± 37.26
LV EF, %, M ± SD	65.51 ± 6.94
LVH, n (%)	49 (51)

Abbreviation: *HDL-c: high-density lipoprotein cholesterol; IQR: interquartile range; LDL-c: low-density lipoprotein cholesterol; LVEF: left ventricular ejection fraction; LVH: left ventricular hypertrophy; LVM: left ventricular mass; LVMI: left ventricular mass index; M: mean; Me: median; SD: standard deviation.*

Table 3 shows ambulatory BP findings in the total population. Mean 24-hour SBP and DBP were 130.80 ± 17.43 mmHg and 73.73 ± 10.17 mmHg, respectively.

Table 3: Parameters of 24-hour ambulatory blood pressure findings of studied participants

Variable	Total (n=96)
24-hour mean	
• Systolic BP, mmHg, M ± SD	130.80 ± 17.43
• Diastolic BP, mmHg, M ± SD	73.73 ± 10.17
• Heart rate, bpm, M ± SD	74.33 ± 12.54
Awake mean	
• Systolic BP, mmHg, M ± SD	131.10 ± 17.52
• Diastolic BP, mmHg, M ± SD	73.76 ± 10.39
Sleep mean	
• Systolic BP, mmHg, M ± SD	128.76 ± 19.77
• Diastolic BP, mmHg, M ± SD	73.24 ± 10.93

Abbreviation: *DBP: systolic blood pressure; M: mean; SBP: systolic blood pressure; SD: standard deviation*

3.2. BP Profiles and correlation with cardiovascular risk factors

The prevalence of masked hypertension was observed in 12 (12.5%) patients. MBPS was observed in 39 patients (40.6%), and 36 patients (37.5%) had ISH.

Nocturnal BP profiles showed dipper pattern in 13 patients (13.5%) (both systolic and diastolic), non-dipper pattern in 51 patients (53.1%) (systolic and/or diastolic), and riser pattern in 54 patients (56.3%) (systolic and/or diastolic) (Fig. 1). Extreme dipper pattern was not observed.

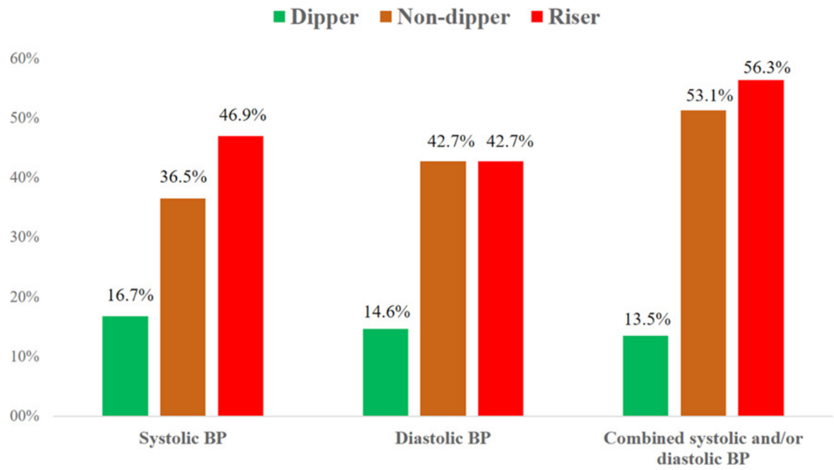

Figure 1: Prevalence of different circadian blood pressure patterns in elderly hypertensive patients
Abbreviation: BP: blood pressure

Univariate correlation analysis of mean 24-hour SBP and DBP was shown in Table 4. There were significant correlations between mean 24-hour SBP with age (r = 0.229), BMI (r = 0.212), waist circumference (r = 0.226), creatinine level (r = 0.207) and dyslipidemia (r = 0.223). Mean 24-hour DBP was significantly with BMI (r = 0.294). Office systolic and diastolic BP were not correlated with any of tested variables (all $p > 0.05$).

Table 4: Correlations between office and ambulatory mean 24-hour systolic and diastolic blood pressure with cardiovascular risk factors

Variable	Office SBP		Office DBP		24-hour mean SBP		24-hour mean DBP	
	r	P-value	r	P-value	r	P-value	r	P-value
Age, years	0.065	0.528	-0.124	0.228	0.229	0.025	-0.104	0.313
BMI, kg/m^2	-0.073	0.478	0.110	0.285	0.212	0.039	0.289	0.004
Diabetes mellitus	0.183	0.074	-0.006	0.951	-0.068	0.509	-0.095	0.356
Smoking	-0.105	0.309	-0.024	0.818	-0.085	0.409	0.003	0.976
Dyslipidemia	0.133	0.196	0.072	0.486	0.223	0.029	0.156	0.128
Waist circumference, cm	-0.113	0.272	0.051	0.623	0.226	0.027	0.194	0.058
Creatinine, µmol/L	0.024	0.816	-0.056	0.588	0.207	0.043	-0.007	0.945
Estimated GFR, ml/min/1.73 m^2	0.085	0.411	0.089	0.388	0.191	0.063	0.001	0.991
Glucose, mmol/L	-0.140	0.174	-0.073	0.482	0.147	0.154	0.155	0.133

Variable	Office SBP		Office DBP		24-hour mean SBP		24-hour mean DBP	
	r	P-value	r	P-value	r	P-value	r	P-value
Total cholesterol, mmol/L	0.014	0.892	0.001	0.992	0.059	0.565	0.130	0.208
Triglycerides, mmol/L	-0.157	0.126	-0.086	0.406	0.036	0.729	0.068	0.509
HDL-c, mmol/L	0.100	0.331	0.050	0.631	0.065	0.526	0.069	0.505
LDL-c, mmol/L	-0.022	0.830	-0.050	0.627	0.074	0.476	0.123	0.232
LVM, g	-0.018	0.865	0.095	0.357	0.042	0.686	-0.006	0.952
LVMI, g/ m^2	0.006	0.951	0.109	0.289	0.048	0.640	0.004	0.966
LVH	0.034	0.742	-0.003	0.980	-0.076	0.461	-0.045	0.665

Abbreviation: *BMI: body mass index;GFR: glomerular filtration rate; HDL-c: high-density lipoprotein cholesterol; LDL-c: low-density lipoprotein cholesterol; LVH: left ventricle hypertrophy; LVM: left ventricular mass; LVMI: left ventricular mass index.*

IV. DISCUSSION

In this study, conducted on elderly high-risk hypertensive patients receiving treatment under routine daily practice, we revealed distinct BP phenotypes and their association with cardiovascular risk factors when compared to office BP measurements. These findings underscore the value of ABPM in assessing BP phenotypes in elderly high-risk hypertensive patients, which were associated with poor prognosis [16,17].

In our study, we found a high prevalence of ISH and MBPS rate, accounting for 37.5% and 40.6% respectively. As individuals age, systolic BP increases linearly, while diastolic BP exhibits an inflection point around the fifth or sixth decade of life, transitioning from a linear increase to a gradual decrease [18]. ISH was the most common cause of elevated BP in the older population [19]. Data from the National Health and Nutrition Examination Survey 1999 - 2010, involving 24,653 participants aged 18 years or older, revealed an overall ISH prevalence of 29.4% among the untreated older age group (≥ 60 years), compared to 6.0% in individuals aged 40-59 years and 1.8% in those aged 18 - 39 years [19]. Older adults with ISH face a significantly greater risk of cardiovascular mortality compared to individuals with normal BP [16]. The association between the timing of cardiovascular events and the circadian variation in BP was reported in previous studies [17,20]. In a study involving elderly hypertensive patients, Kario et al. were the first to demonstrate that an exaggerated MBPS measured using ABPM was independently associated with an increased risk of stroke [20]. Specifically, patients in the highest 10% of MBPS (≥ 55 mm Hg) had a 2.7-fold higher risk of future stroke compared to those with a morning surge below 55 mm Hg [20]. Pierdominico et al. found that stroke, as well as coronary events, were associated with elevated MBPS, independent of 24-hour BP levels [17]. A 10 mm Hg increase in early MBPS correlated with a 24% higher stroke risk (p = 0.004) [17].

In our study, the prevalence of masked uncontrolled hypertension (MUCH) among older hypertensive patients was 12.5%. Its prevalence is not well known, but it has been suggested to be about 10 - 20% of the general population [21,22]. Bobrie et al. in a study carried out in 4939 patients older than 65 years, reported a prevalence of MUCH of 9.4% [23]. In a study conducted by Shi et al. on 760 hypertensive patients aged 50 - 75 years, MUCH was observed in 236 patients (31%). MUCH was found to be independently associated with a higher prevalence of cardiovascular diseases, including coronary heart disease, ischemic stroke, and chronic heart failure, with an odds ratio of 1.38 (95% confidence interval [CI] 1.17 - 1.62, $p < 0.05$) [24]. A meta-analysis including 30,352 hypertensive patients from 11 studies, including 6 studies using ABPM (n = 12,610) and 5 studies using home BP measurement (n = 17,742), further supported these findings [22]. Compared to patients with controlled hypertension, patients with MUCH showed an increased risk of cardiovascular events (stroke, coronary artery disease, heart failure, and peripheral revascularization) and all-cause mortality (hazard ratio, 1.8; 95% CI, 1.6 - 2.1) [25].

In our study, more than half of elderly patients with hypertension were classified as either non-dippers or risers. In older hypertensive patients, one age-related abnormality in BP patterns is the lack of a nocturnal BP dip, resulting in a higher proportion of patients classified as non-dippers compared to younger subjects [26]. In a study involving 42,947 hypertensive patients [27], the patients were divided into two groups: previously untreated (n = 8,384) and treated (n = 34,563). The prevalence of non-dipping was 41% in the untreated group and 53% in the treated group. Furthermore, the prevalence of patients classified as risers was 6.0% and 13.5% respectively [27]. Another study followed 575 hypertensive patients aged ≥ 50 years old for an mean duration of 41 months [28]. The distribution of dipping patterns in these patients was as follows: extreme-dippers (17%), dippers (40%), non-dippers (32%), and risers (11%). The risers exhibited the highest incidence of strokes (22%) compared to 6.1% and 7.6% in the dipper and non-dipper groups, respectively. These alterations in circadian patterns among elderly hypertensive patients are associated with an increased cardiovascular events [29].

In our study, we observed that BP profiles obtained from ABPM were stronger associations with other cardiovascular risk factors compared to office BP measurements. Specifically, BMI showed a positive correlation with both 24-hour systolic and diastolic BP. These findings are consistent with previous studies [30 - 32]. The stronger correlations between mean ambulatory 24-hour systolic BP and risk factors such as age, BMI, waist circumference, and dyslipidemia suggest that a significant portion of BP elevation in this population is attributable to lifestyle factors. Therefore, interventions aimed at controlling BP should prioritize lifestyle modifications. Furthermore, we observed a significant relationship between creatinine levels, as a marker of renal function, and 24-hour systolic BP. This suggests that sustained high BP may have an impact on kidney function. Overall, our findings highlight the importance of considering ABPM measurements for a more comprehensive assessment of BP and its association with cardiovascular risk factors. Lifestyle modifications and monitoring renal function may be crucial aspects of BP management in this population.

Our study has several limitations. First, the cross-sectional design of the study restricts our ability to establish causal relationships between variables. Second, the classification of individuals as dippers or non-dippers based on a single 24-hour ABPM measurement may not accurately capture their long-term blood pressure patterns. However, the concordance of results obtained by examining the night-to-day BP ratio as a continuous variable adds scientific validity to our findings.

V. CONCLUSION

Our study revealed that elderly high-risk hypertensive patients exhibited a higher prevalence of ISH, MBPS, and non-dipping patterns. Furthermore, we found significant associations between mean 24-hour systolic and diastolic BP and cardiovascular risk factors. These findings underscore the importance of comprehensive 24-hour ABPM in this population for effective management and cardiovascular risk assessment.

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