

ORIGINAL PAPER

MORNING BLOOD PRESSURE SURGE AND ASSOCIATED FACTORS IN PATIENTS WITH PRIMARY HYPERTENSION

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ABSTRACT

Introduction. Patients with arterial hypertension have a higher rate of morning blood pressure surge (MBPS) than non-hypertensive patients. MBPS increases the risk of stroke, myocardial infarction, sudden cardiac death, arterial stiffness, left ventricular hypertrophy, carotid atherosclerosis, and vascular inflammation. The prevalence and predictors of MBPS may vary significantly between geographic regions.

The objective of the study was to determine the incidence of MBPS and associated factors in patients with primary hypertension.

Material and methods. A cross-sectional descriptive study was conducted in patients ≥ 35 years old, diagnosed with primary arterial hypertension, and hospitalized in the Department of Cardiology of Thanh Vu Hospital, Bac Lieu, Vietnam, between March 2019 and May 2020.

Results. Among 126 hypertensive patients, 80 had MBPS (63.5%): 66 had systolic MBPS (52.4%), 65 had diastolic MBPS (51.6%), and 51 had both systolic and diastolic MBPS (40.5%). Nocturnal hypertension, left ventricular hypertrophy, and stroke were statistically associated with MBPS.

RÉSUMÉ

La poussée matinale de la pression artérielle et les facteurs associés chez les patients ayant une hypertension primaire

Introduction. Les patients souffrant d'hypertension artérielle ont un taux plus élevé d'augmentation de la pression artérielle matinale (poussée matinale, PM) que les patients non hypertendus. La PM augmente le risque d'accident vasculaire cérébral, d'infarctus du myocarde, de mort subite d'origine cardiaque, de rigidité artérielle, d'hypertrophie ventriculaire gauche, d'athérosclérose carotidienne et d'inflammation vasculaire. La prévalence et les prédictors de PM peuvent varier considérablement entre les régions géographiques.

L'objectif de l'étude était de déterminer l'incidence de la PM et des facteurs associés chez les patients souffrant d'hypertension primaire.

Matériel et méthodes. Une étude descriptive transversale a été menée chez des patients âgés de 35 ans et plus, diagnostiqués avec une hypertension artérielle primaire, et hospitalisés dans le service de cardiologie de l'hôpital de Thanh Vu, Bac Lieu, Vietnam, entre mars 2019 et mai 2020.

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Conclusions. Since there is a high prevalence of MBPS, associated with multiple complications in patients with grade 2 or 3 hypertension, 24-hour ambulatory blood pressure measurement must be used in clinical practice in this group of patients, to ensure the timely detection and treatment of MBPS.

Keywords: morning blood pressure surge, primary hypertension, left ventricular hypertrophy, stroke.

Résultats. Parmi 126 patients hypertendus, 80 avaient une PM (63,5%): 66 avaient une PM systolique (52,4%), 65 avaient une PM diastolique (51,6%) et 51 avaient à la fois une PM systolique et diastolique (40,5%). L'hypertension nocturne, l'hypertrophie ventriculaire gauche et les accidents vasculaires cérébraux étaient statistiquement associés avec PM.

Conclusion. Étant donné qu'il existe une prévalence élevée de la PM, associée à de multiples complications chez les patients souffrant d'hypertension de grade 2 ou 3, la mesure ambulatoire de la pression artérielle sur 24 heures doit être utilisée en pratique clinique dans ce groupe de patients, afin d'assurer la détection et le traitement en temps opportun de la PM.

Mots-clés: poussée matinale de la pression artérielle, hypertension primaire, hypertrophie ventriculaire gauche, accident vasculaire cérébral.

INTRODUCTION

Arterial hypertension was the leading cause of death in approximately 10 million people in 2015, of whom 4.9 million died of coronary heart disease, and 3.5 million of a stroke¹. Hypertension can also cause heart failure, atrial fibrillation, chronic kidney disease, peripheral vascular disease, and impaired cognitive function¹. Although numerous advances have been made in the diagnosis, treatment, and management of hypertension, its prevalence has been increasing and the rate at which blood pressure control is achieved is not adequate. For instance, the incidence of hypertension in adults in the late 1980s was 11%, increasing to 25.1% in 2008, and further to 47.3% in 2016. Of these patients, 39.1% did not acknowledge that they had hypertension, and 69% did not have an acceptable level of blood pressure control^{2,3}.

Morning blood pressure surge (MBPS) is defined as a difference between the mean systolic blood pressure in the 2 hours after the patient first woke and the lowest systolic blood pressure at night of ≥ 20 mmHg and/or a difference between the mean diastolic blood pressure in the 2 hours after the patient first woke and the lowest diastolic blood pressure at night of ≥ 15 mmHg⁴. According to Luo et al., hypertensive patients have a higher incidence of MBPS compared to non-hypertensive patients⁵. Further, MBPS increases the risk of stroke by 49%, of myocardial infarction by 40%, and of sudden cardiac death by 29%⁶. MBPS is also associated with arterial stiffness, left ventricular hypertrophy, carotid arteries atherosclerosis, and vascular inflammation⁷. A study by Amodeo et al., on 632 hypertensive patients in Brazil, showed that patients with a MBPS of ≥ 41 mmHg had

a 3.35 increased risk of death⁸. Therefore, to prevent complications and reduce mortality in hypertensive patients, it is crucial to control the blood pressure throughout the day, especially the MBPS.

The incidence of MBPS varies significantly by country. In China, the reported rate of MBPS in hypertensive patients adhering to treatment was 41%, and 53% for those not adhering to treatment⁹. In India, the rate of MBPS in patients with type 2 diabetes was 88.52%¹⁰. In Pakistan, an incidence rate of 80.5% was reported¹¹. In Vietnam, a study reported that 25% of patients with cerebral infarction, but without hypertension, had MBPS, whereas in hypertensive patients, this percentage was 62.1%¹². Other studies conducted in Vietnam reported MBPS rates of 69.7%¹³ and 72.2%¹⁴. These studies have further identified number of factors associated with MBPS, including age over 60 years⁷, being a member of certain ethnic groups¹⁵, history of hypertension, elevated daytime systolic blood pressure⁵, left ventricular hypertrophy¹⁶, coronary heart disease¹⁷, heart failure and peripheral vascular disease¹⁸, stroke⁶, type 2 diabetes¹⁰, smoking⁷, alcohol consumption, being overweight or obese, stress, carotid atherosclerosis⁶, and poor control of serum glycemia¹⁰. Further, MBPS appears to be more prevalent in the winter season, and on the first day of the week (i.e. Monday).

In 2018, the Hypertension and Organ Protection (HOPE) Asia Network stated the importance of screening, diagnosis, and treatment in patients with MBPS⁶. The predictors of MBPS may vary significantly between geographic regions and patients' socio-demographic characteristics. Therefore, this study was proposed and conducted to contribute to

Table 1. The general characteristics of the group of study (n = 126)

	Frequency (n)	Percentage (%)
Sex		
Male	40	31.7
Female	86	68.3
Age group (years)		
35-59	34	27
60+	92	73
Occupation		
Officer	7	5.6
Trader	11	8.7
Housewife	21	16.7
Farmer	25	19.8
Unemployment	62	49.2
Time since first diagnosis of hypertension (years)		
<1	10	7.9
1-5	36	28.6
>5	80	63.5
Cardiovascular risk factors		
Sedentary lifestyle	90	71.4
Dyslipidemia	84	66.7
Overweight-obesity	76	60.3
Smoking	42	33.3
Type-2 diabetes	32	25.4

the effective screening and treatment of MBPS in the Mekong Delta, specifically in Bac Lieu.

THE OBJECTIVE OF THE STUDY was to determine the MBPS incidence and associated factors in patients with primary hypertension.

MATERIAL AND METHODS

Study design and setting

A cross-sectional descriptive study was conducted in patients aged 35 years and over, diagnosed with primary hypertension and hospitalized in the Department of Cardiology of Thanh Vu Medic Hospital, Bac Lieu, Vietnam, between March 2019 and May 2020. The inclusion criteria were: patients diagnosed with hypertension of grade 2 or 3 and/or who had been prescribed antihypertensive drug therapy at the time of hospitalization. Hypertension grade 2 or higher, according to the Vietnam Heart Association, is diagnosed when the systolic blood pressure is ≥ 160 mmHg and/or the diastolic blood pressure is ≥ 100 mmHg¹. A convenience sampling method was used during the study period until sufficient patients were recruited. The sample size was calculated using the following equation:

$$n = \frac{Z_{1-\frac{\alpha}{2}}^2 \cdot \frac{a}{2} \cdot p \cdot (1 - p)}{c^2}$$

where, n is the number of research subjects; a is the probability of type 1 error ($a = 0.05$ in this study), Z is the value from the normal distribution ($Z = 1.96$), c is the acceptable error ($c = 0.08$ in this study), and p is the MBPS rate in hypertensive patients. According to a study by Nguyen Thanh Nam (2018), p was reported to be 72.2%¹⁴. Therefore, the sample size, n , for this study was calculated to be 121 patients.

The general patients' characteristics were recorded in terms of (1) socio-demographic characteristics, namely the patient's sex, age, occupation, and when the hypertension had first been detected; (2) cardiovascular risk factors, namely a sedentary lifestyle, dyslipidemia (defined based on the Vietnam Ministry of Health Guidelines¹⁹), being overweight or obese (based on body mass index (BMI))²⁰, the smoking status, whether or not they had type-2 diabetes, and the blood pressure over a 24-hour period (day-time hypertension, morning hypertension); and (3) any identified complications of hypertension, namely left ventricular hypertrophy (based on established criteria^{2,21}), microproteinuria (based on the Vietnam Society of Endocrinology and Metabolism criteria¹⁹),

Table 2. Factors associated with morning blood pressure surge (MBPS)

	MBPS n (%)		Total n (%)	OR (95% CI)
	Yes	No		
Overweight/obese				
Yes	51 (67.1)	25 (32.9)	76 (60.3)	1.5 (0.7-3.1)
No	29 (58)	21 (42)	50 (39.7)	
Type-2 diabetes				
Yes	18 (56.3)	14 (43.8)	32 (25.4)	0.6 (0.3-1.5)
No	62 (66)	32 (34)	94 (74.6)	
24-hour hypertension				
Yes	67 (67.7)	32 (32.3)	99 (78.6)	2.26 (0.95-5.3)
No	13 (48.1)	14 (51.9)	27 (21.4)	
Nocturnal hypertension				
Yes	62 (91.2)	6 (8.8)	68 (54)	22.9 (8.4-62.8)**
No	18 (31)	40 (69)	58 (46)	
Left ventricular hypertrophy				
Yes	38 (79.2)	10 (20.8)	48 (38.1)	3.26 (1.4-7.4)**
No	42 (53.8)	36 (46.2)	78 (61.9)	
Microproteinuria				
Yes	32 (72.7)	12 (27.3)	44 (34.9)	1.9 (0.8-4.2)
No	48 (58.5)	34 (41.5)	82 (65.1)	
Carotid atherosclerosis				
Yes	39 (57.4)	29 (42.6)	68 (54)	0.6 (0.27-1.2)
No	41 (70.7)	17 (29.3)	58 (46)	
Stroke				
Yes	27 (84.4)	5 (15.6)	32 (25.4)	4.18 (1.5-11.8)**
No	53 (56.4)	41 (43.6)	94 (74.6)	

Note: ** p-value < 0.01 at the 5% level of significance.

carotid atherosclerosis (confirmed on ultrasound¹⁶), and stroke.

MBPS definition

Patients with grade 2 and 3 hypertension underwent continuous ambulatory blood pressure monitoring (ABPM) for 24 hours. MBPS was evaluated in all the patients. The mean blood pressure in the 2 hours after waking was defined as the average value of four measurements taken at 30-minute intervals after the patient first awake⁶. The lowest blood pressure at night was defined as the average of three measurements, where one was the lowest value throughout the night, and the other two were the values at 30 minutes before and after this lowest value measurement¹⁶. In this study, electrocardiography (ECG) and transthoracic echocardiography were performed in all the patients.

Ethical considerations

The research proposal was approved by the Medical Ethics Council of Can Tho University of Medicine and Pharmacy, Can Tho city, Vietnam

(approval number 247/HĐĐĐ-PCT, March 13, 2019). The research subjects were clearly explained the purpose of the study and the processes involved, and voluntarily participated in the study. All patients' information was kept confidential. All patients signed a written informed consent form agreeing to voluntarily take part in the study.

Statistical analysis

Data were processed using the software SPSS 18.0. Information was presented as frequencies (n), percentages (%), means, and standard deviations. The relationships between variables were determined using chi-squared tests or Fisher's tests (where appropriate). Differences were considered statistically significant at a threshold of p < 0.05.

RESULTS

Patients' characteristics

The patients' characteristics are presented in Table 1. A total of 126 hypertensive patients were

Table 3. Factors associated with systolic morning blood pressure surge (MBPS).

	Systolic MBPS n (%)		Total n (%)	OR (95% CI)
	Yes	No		
Overweight/obese				
Yes	42 (55.3)	34 (44.7)	76 (60.3)	1.34 (0.6-2.7)
No	24 (48)	26 (52)	50 (39.7)	
Type-2 diabetes				
Yes	17 (53.1)	15 (46.9)	32 (25.4)	1.04 (0.46-2.3)
No	49 (52.1)	45 (47.9)	94 (74.6)	
24-hour hypertension				
Yes	55 (55.6)	44 (44.6)	99 (78.6)	1.8 (0.7-24.3)
No	11 (40.7)	16 (59.3)	27 (21.4)	
Nocturnal hypertension				
Yes	50 (73.5)	18 (26.5)	68 (54)	7.29 (3.3-16)**
No	16 (27.6)	42 (72.4)	58 (46)	
Left ventricular hypertrophy				
Yes	31 (64.6)	17 (35.4)	48 (38.1)	2.2 (1.4-7)*
No	35 (44.9)	43 (55.1)	78 (61.9)	
Microproteinuria				
Yes	29 (65.9)	15 (34.1)	44 (34.9)	2.35 (1.1-5)*
No	37 (45.1)	45 (54.9)	82 (65.1)	
Carotid atherosclerosis				
Yes	31 (45.6)	37 (54.4)	68 (54)	0.55 (0.27-1.1)
No	35 (60.3)	23 (39.7)	58 (46)	
Stroke				
Yes	24 (75)	8 (25)	32 (25.4)	3.71 (1.5-9)**
No	42 (44.7)	52 (55.3)	94 (74.6)	

Note: * p-value < 0.05 at the 5% level of significance; ** p-value < 0.01 at the 5% level of significance

included in the study. The largest number of patients (68.3%) were women, aged ≥ 60 years-old (73%), had hypertension for over 5 years (63.5%), and had cardiovascular risk factors such as a sedentary life-style (71.4%), dyslipidemia (66.7%), and overweightness/obesity (60.3%). The results of 24-hour ABPM showed that the average 24-hour systolic blood pressure was 131.1 ± 5.7 mmHg, and the diastolic blood pressure 80.67 ± 4.16 mmHg.

MBPS incidence rate

Among the 126 hypertensive patients, 80 experienced a MBPS (63.5%). Of these, 66 had systolic MBPS (52.4% of the group of study), 65 had diastolic MBPS (51.6% of the group of study), and 51 had both systolic and diastolic MBPS (40.5% of the group of study). Of patients with MBPS, the majority were ≥ 60 years-old (72.5%). The analysis of the 24-hour ABPM showed that the rates of daytime hypertension and morning hypertension were 68.8% and 55%, respectively.

Factors associated with MBPS

Table 2 presents the various factors associated with MBPS. Nocturnal hypertension, left ventricular hypertrophy, and stroke were statistically associated with MBPS. Patients with nocturnal hypertension, left ventricular hypertrophy, or stroke had a higher rate of MBPS than other patients (91.2% vs. 31%, $p < 0.01$; 79.2% vs. 53.8%, $p < 0.01$; and 84.4% vs. 56.4%, $p < 0.01$, respectively). No significant associations were found between MBPS and overweight/obesity, type-2 diabetes, 24-hour hypertension, microproteinuria, or carotid atherosclerosis.

The factors associated with systolic MBPS and diastolic MBPS are shown in Tables 3 and 4, respectively. Nocturnal hypertension, left ventricular hypertrophy, and stroke were more prevalent in patients with either systolic or diastolic MBPS. Conversely, microproteinuria was associated only with systolic MBPS, and overweightness/obesity and 24-hour hypertension were associated only with diastolic MBPS.

Table 4. Factors associated with diastolic morning blood pressure surge (MBPS).

	Diastolic MBPS n (%)		Total n (%)	OR (95% CI)
	Yes	No		
Overweight/obese				
Yes	45 (59.2)	31 (40.8)	76 (60.3)	2.18 (1.4-5)*
No	20 (40)	30 (60)	50 (39.7)	
Type-2 diabetes				
Yes	17 (53.1)	15 (46.9)	32 (25.4)	1.1 (0.49-2.4)
No	48 (51.1)	46 (48.9)	94 (74.6)	
24-hour hypertension				
Yes	57 (57.6)	42 (42.4)	99 (78.6)	3.2 (1.29-8)**
No	8 (29.6)	19 (70.4)	27 (21.4)	
Nocturnal hypertension				
Yes	55 (80.9)	13 (19.1)	68 (54)	20.3 (8.2-50)**
No	10 (17.2)	48 (82.8)	58 (46)	
Left ventricular hypertrophy				
Yes	33 (68.8)	15 (31.2)	48 (38.1)	3.16 (1.5-6.75)**
No	32 (41)	46 (59)	78 (61.9)	
Microproteinuria				
Yes	24 (54.5)	20 (45.5)	44 (34.9)	1.2 (0.5-2.5)
No	41 (50)	41 (50)	82 (65.1)	
Carotid atherosclerosis				
Yes	34 (50)	34 (50)	68 (54)	0.9 (0.4-1.7)
No	31 (53.4)	27 (46.6)	58 (46)	
Stroke				
Yes	22 (68.8)	10 (31.2)	32 (25.4)	2.61 (1.1-6.1)*
No	43 (45.7)	51 (54.3)	94 (74.6)	

Note: * p-value < 0.05 at the 5% level of significance; ** p-value < 0.01 at the 5% level of significance.

DISCUSSION

Most of the hypertensive patients in this study were elderly and had cardiovascular risk factors and other comorbidities, thus, an effective control of blood pressure is essential to prevent complications. In clinical practice, physicians need to pay careful consideration to patients' counseling, to control and treat cardiovascular risk factors.

In our study, 63.5% of hypertensive patients had a MBPS, which was similar to the findings of a study conducted in Luong Cong Thuc and Luu Quang Minh (69.7%)¹³. Similarly, a survey conducted by Cao Thuc Sinh found a rate of MBPS in hypertensive patients with ischemic stroke of 67.3%¹². Li et al. found a MBPS rate in hypertensive patients of 64.3% across Denmark, Belgium, Russia, Italy, Poland, Japan, China, and Uruguay²². However, our rate was higher than that reported in Korea (51.5%)²³, Europe (40%)²⁴, and Japan (40.3%)¹⁵.

Our study found that nocturnal hypertension was associated with MBPS, systolic MBPS and

diastolic MBPS, consistent with the findings of Ye Runyu et al.²⁵, and Luo Yu et al.²³. Therefore, nocturnal hypertension and MBPS appear to be positively correlated. Similarly, left ventricular hypertrophy was also associated with MBPS, as well as systolic and diastolic MBPS. Our results correspond with those of previous studies^{7,25,26}. As hypertension is associated with elevated pressure in the heart, the myocardium responds by thickening the ventricular wall to provide a greater contraction force, thereby overcoming peripheral resistance and maintaining cardiac output, resulting in hypertrophy²⁷. Previous studies showed that MBPS was significantly correlated with left ventricular mass index and the ratio of the early (E) to late (A) ventricular filling velocities (the E/A ratio) in the presence of diastolic dysfunction. Additionally, hypertensive patients with MBPS exhibited longer QTc durations in the morning compared with patients without MBPS^{7,12}. This long QTc duration, together with prolonged sympathetic nerve dysfunction, act to further exacerbate MBPS^{7,12}.

Stroke is also associated with both MBPS, and systolic or diastolic MBPS. Our results were similar with those of previous studies^{12,23,28,29}. As 47% of stroke events (ischemic stroke and hemorrhagic stroke combined) occur in the early morning¹², MBPS may be the underlying cause, through damages of the cerebral vessels walls. If the lesion is small, platelets and fibrin will form a blood clot. This series of events, combined with an increase in low-density lipoprotein cholesterol (LDL-c), thicken and narrow the vessel wall, eventually causing blood vessel occlusion, leading to cerebral infarction.

Associations between MBPS and body weight (overweightness, obesity) have been previously reported^{15,30-31,32}. Further, the relationship between MBPS and 24-hour ABPM data has also been investigated^{11,16}. We found that overweightness/obesity and elevated blood pressure over a 24-hour period were only associated with diastolic MBPS, but not systolic or systolo-diastolic MBPS. Microproteinuria, the presence of proteins (mainly albumin) in the urine because of glomerular endothelial cell dysfunction, was also associated with systolic MBPS. In hypertensive patients, microproteinuria is a strong and independent predictor of cardiovascular risk, with an incidence as high as 58.4%³³, thus it must be closely monitored. It was previously found that patients with type-2 diabetes and MBPS had higher microproteinuria than the non-MBPS group⁷. This was interpreted as being due to MBPS, that increases the efferent arteriolar pressure of the glomeruli, causing microproteinuria⁷. Thus, controlling MBPS may in turn reduce microproteinuria⁵.

CONCLUSIONS

This study reported the incidence of MBPS and associated factors in patients with primary hypertension in Bac Lieu, Vietnam. Nocturnal hypertension, left ventricular hypertrophy, and stroke were significantly associated with MBPS. MBPS was common in our group of hypertensive patients and was found to be associated with many complications in patients with grade 2 and 3 hypertension. 24-hour ABPM must be used in these patients, to improve the timely detection and treatment of MBPS.

Author Contributions:

Conceptualization, T.K.N. and D.L.N.; *methodology*, T.K.N.; *software*, D.L.N.; *validation*, D.L.N. and T.T.N.D.; *formal analysis*, D.L.N.; *investigation*, D.L.N.; *resources*, T.K.N.; *data curation*, T.T.N.D. and H.H.N.; *writing—original draft preparation*, V.D.T. and R.S.D.; *writing—review and editing*, R.S.D. and V.D.T.; *visualization*,

T.T.N.D. and H.H.N.; *supervision*, T.K.N.; *project administration*, T.K.N.. All the authors have read and agreed with the final version of the article.

Compliance with Ethics Requirements:

“The authors declare no conflict of interest regarding this article“

“The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008(5), as well as the national law. Informed consent was obtained from all the patients included in the study“

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Availability of data and materials

Data and materials used and/or analyzed during the current study are available from the corresponding author on request.

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