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Role of ambulatory blood pressure monitoring in prediction of cardiovascular risk: a retrospective study and literature review

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Summary

There is growing evidence that nocturnal ambulatory blood pressure (BP) is a better predictor of cardiovascular outcome than diurnal BP in patients with hypertension, but data in the literature on the prognostic significance of the nocturnal dipping pattern are not consistent and independence from 24-hour BP has not often been studied. The aim of our research is to identify the dipping pattern of nocturnal BP among normotensive young people and to determine the relationship between dipping categories on the one side and risk factors of cardiovascular disease (CVD) on the other side. In our retrospective study, we examined 103 normotensive young people (mean age 28.5 years) without CVD. The 24-hour ambulatory blood pressure monitoring (ABPM) was used to estimate nocturnal BP and its dipping pattern. A questionnaire was used to determine the patients' life pattern and cardiovascular risk factors. Results indicate that mean nocturnal BP among men is 10 mmHg higher than among women, and obese patients have higher mean nocturnal BP than patients with normal body mass index (BMI) (127±12/74±6 vs. 104±11/59±8 mmHg; P=0.000). The nocturnal BP decrease among smokers is lower than among nonsmokers (8±8 vs. 13±6 %; P<0.05) and among patients involved in sport, the decrease is higher than among the less sporty patients (14±6 vs. 10±7 %; P=0.03). We concluded that there are direct relations between cardiovascular risk factors and nocturnal BP, and that dipping categories can be determined by a patient's lifestyle.

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Keywords
Arterial hypertension, ambulatory blood pressure monitoring, cardiovascular risk, nocturnal BP, dippers, non-dippers

Introduction

Hypertension can progress without manifestations for 15–20 years of clinical course, but later, left ventricular hypertrophy, hypertensive nephropathy, retinopathy and other complications are most likely to develop. There are direct relations between the value of arterial BP (ABP) and the development of CVD – an increase in either systolic or diastolic BP significantly rises the risk of CVD (beginning from 115/75 mmHg, the risk of CVD rises with every 20/10 mmHg). If untreated, hypertension can lead to a fatal outcome: half of all untreated hypertensive patients could have died from coronary heart disease (CHD) and heart failure, one third of the patients from stroke, and 10–15% could have died from renal failure [1].

There is growing evidence that nocturnal ambulatory BP is a better predictor of cardiovascular outcome than diurnal BP in patients with hypertension. But data in the literature on the prognostic significance of the nocturnal dipping pattern are not consistent and independence from 24-hour BP has not often been studied. The dipping pattern and the night–day BP ratio significantly and independently predict mortality and cardiovascular events in hypertensive patients without history of main CVD [2].

Ambulatory blood pressure monitoring

Ambulatory blood pressure monitoring (ABPM) is a fully automated technique in which multiple BP measurements are taken at regular intervals (usually every 15–30 minutes) over a 24–48-hour period, providing a continuous BP record during patient's normal daily activities. Some experts advocate the use of 24-hour ABPM for all first diagnoses of hypertension and for treatment decision-making [3]. The use of ABPM can improve BP monitoring so that treatment can be optimized more rapidly and more patients can achieve BP targets with appropriate therapy. ABPM may lead to better patient outcomes while requiring less-intensive drug regimens to maintain BP control and reducing treatment costs. By more accurately and reliably measuring BP, especially circadian changes, ABPM has been shown to predict cardiovascular morbidity and mortality and end organ damage. ABPM is especially beneficial for patients whose hypertension is difficult to diagnose, including the elderly, patients with diabetes, and individuals with resistant hypertension. ABPM is also beneficial for predicting disease severity and prognosis among patients with chronic renal disease, a condition associated with significant cardiovascular risk [4].

The use of 24-hour ABPM has not been widely integrated into main hypertension guidelines. Most guidelines recommend the use of ABPM only in selected cases. For example, the 2013 *ESH/ESC* Guidelines for the management of arterial hypertension highlighted the potential value of ABPM in white-coat hypertension (BP raises when measured in the office but normal when it is self-measured at home), masked hypertension, suspected pre-eclampsia in pregnancy, labile hypertension and hypotensive episodes (Table 1).

Table 1. **Clinical indications for out-of-office blood pressure measurementfor diagnostic purposes**
(from 2013 ESH/ESC Guidelines forthe management of arterial hypertension)
Clinical indications for HBPM or ABPM

Clinical indications for HBPM or ABPM
• **Suspicion of white-coat hypertension**
– Grade I hypertension in the office
– High office BP in individuals without asymptomatic organ damage and at low total C V risk
• Suspicion of masked hypertension
– High normal BP in the office
– Normal office BP in individuals with asymptomatic organ damage or at high total CV risk
• Identification of white-coat effect in hypertensive patients
• Considerable variability of office BP over the same or different visits
• Autonomic, postural, post-prandial, siesta- and drug-induced hypotension
• Elevated office BP or suspected pre-eclampsia in pregnant women
• Identification of true and false resistant hypertension Specific indications for ABPM
Specific indications for ABPM
• Marked discordance between office BP and home BP
• Assessment of dipping status
• Suspicion of nocturnal hypertension or absence of dipping, such as in patients with sleep apnoea, CKD, or diabetes
• Assessment of BP variability

ABPM, ambulatory blood pressure monitoring; BP. blood pressure; CKD, chronic kidney dsease; CV. cardiovascular; HBPM, home blood pressure monitoring.

Interpretation of ABPM

Unique data provided by ABPM include: 24-hour average BP; diurnal (awake) BP; nocturnal (asleep) BP; systolic BP load; diastolic BP load; and nocturnal BP dipping. Dipping is discussed in more detail below.

Regarding the definition of hypertension, after reviewing multiple large cohorts of individuals who underwent ABPM, consensus has been reached on the thresholds used to define normotension and hypertension based upon the data obtained from ABPM [5]. These thresholds depend upon the time span over which BP was measured (Table 2).

Table 2. **Definitions of hypertension by office and out-of-office blood pressure levels (from 2013 ESH/ESC Guidelines forthe management of arterial hypertension)**

Category	Systolic BP (mmHg)		Diastolic BP (mmHg)
Office BP	>140	and/or	>90
Ambulatory BP			
Daytime (or awake)	>135	and/or	>85
Nighttime (or asleep)	>120	and/or	>70
24-h	>130	and/or	>80
Home BP	>135	and/or	>85

24-hour average BP – Normotension is defined as a BP less than 130/80 mmHg, and hypertension is defined as a BP greater than or equal to 135/85 mmHg

Diurnal (awake) BP – Normotension is defined as a BP less than 135/85 mmHg, and hypertension is defined as a BP greater than or equal to 140/90 mmHg

Nocturnal (asleep) BP – Normotension is defined as a BP less than 120/70 mmHg, and hypertension is defined as a BP greater than or equal to 125/75 mmHg

In addition to the visual plot, average diurnal, nocturnal and 24-hour BP are the most commonly used variables in clinical practice. Average diurnal and nocturnal BP can be calculated from the diary on the basis of the times of getting up and going to bed. The night-to-day BP ratio represents the ratio between average nocturnal and diurnal BP. BP normally decreases during the night and it is defined as 'dipping'. Although the degree of nocturnal dipping has a normal distribution in a healthy population setting, it is generally agreed that the finding of a nocturnal BP fall of >10% of diurnal values (night-day BP ratio <0.9) will be accepted as an arbitrary cut-off to define subjects as 'dippers'. Recently, more dipping categories have been proposed: absence of dipping, i.e. a nocturnal BP increase (ratio >1.0); mild dipping (0.9 <ratio <1.0); dipping (0.8 <ratio <0.9); and extreme dipping (ratio <0.8).

A number of additional indices may be derived from ABPM recordings [6–12]. They include: BP variability [6], morning BP surge [7,8,12], BP load [9], and the ambulatory arterial stiffness index [10,11]. However, their added predictive value is not yet clear and they should thus be regarded as experimental, with no routine clinical use.

Prediction of cardiovascular risk

A number of studies have suggested that the risk of hypertensive cardiovascular complications correlates more closely with 24-hour, diurnal, or nocturnal ABPM than with the office BP [13–17].

This more accurate assessment of cardiovascular risks with 24-hour monitoring was illustrated in the following studies [14,15,18]:

- In a prospective study with 1,963 hypertensive patients, an increased risk for a new cardiovascular event was observed in patients with a 24-hour ambulatory systolic BP of greater than 135 mmHg (relative risk 1.75, 95% CI 1.15 to 2.63 compared to less than 135 mmHg) [22].
- In two separate community-based studies with 1,700 and 5,292 participants, multivariate analysis demonstrated that ambulatory BP was more predictive of cardiovascular and all-cause mortality than office BP after a mean follow-up of over eight years [14,15].

ABPM also has predictive value in patients with resistant hypertension. At an equivalent level of office BP, patients with higher ambulatory values are at greater cardiovascular risk [19–21].

Progression of kidney disease

A cohort study of 217 patients suggested that elevated BP based on ABPM correlated more strongly with progression to end-stage renal disease (ESRD) than clinic systolic BP [23]. In addition, nocturnal ambulatory BP was a strong predictor of the composite outcome of death and ESRD.

Masked hypertension

From 10 to 40 percent of patients who are normotensive according to conventional clinic measurement are hypertensive according to ABPM [24–27]. This phenomenon is called masked hypertension or isolated ambulatory hypertension. It has only been identified by screening clinical studies since patients who are normotensive by office readings do not typically undergo ambulatory monitoring.

Masked hypertension has been associated with an increased long-term risk of sustained hyperten-

sion and cardiovascular morbidity [26–31]. Because of the risk associated with masked hypertension, ABPM should be considered in patients referred for possible hypertension (for a variety of reasons, such as left ventricular hypertrophy) despite repeatedly normal BP when measured in the clinic.

Nocturnal BP and nondippers

Considerable data suggest that measurement of nocturnal BP yields additional prognostic data in terms of all-cause mortality and cardiovascular events [15,18,32,33]:

– A cohort study of 7,458 patients in six countries from Europe, Asia, and South America found that both diurnal and nocturnal BP predicted all cardiovascular events [32]. Nocturnal BP, adjusted for diurnal BP, predicted total, cardiovascular, and noncardiovascular mortality. In contrast, diurnal BP, adjusted for BP measured during sleep, only predicted noncardiovascular mortality.

– Similar findings were noted in a second cohort of 3,957 patients who underwent ABPM obtained during sleep were more predictive of all-cause mortality than those obtained during waking hours [33].

The average nocturnal BP is approximately 15 percent lower than diurnal values in both normal and hypertensive patients [34]. Failure of the BP to fall by at least 10 percent during sleep is called nondipping. The underlying mechanisms of nondipping are unknown, but intrinsic renal defects may contribute [35–37].

There is evidence suggesting that melatonin may play a role. Independent of the degree of hypertension, nondipping is a risk factor for the development of left ventricular hypertrophy (LVH), heart failure and other cardiovascular complications [13,38–41]. However, extreme dipping (for example, >20 percent nocturnal decline in BP) and a large morning increase in BP are also potentially deleterious [40,42].

Nondipping has also been associated with moderately increased albuminuria (formerly called «microalbuminuria») and faster progression of nephropathy in patients with diabetes mellitus [43,45]. More importantly, nondipping may be a risk factor for decline in glomerular filtration rate, ESRD, and death among patients with chronic kidney disease [23,45]. The presence of sleep apnea should also be considered in nondippers. Whether reversal of nondipping is possible or beneficial is uncertain.

There is growing evidence that nocturnal ambulatory BP is a better predictor of cardiovascular outcome than diurnal BP in patients with hypertension, but data in the literature on the prognostic significance of the nocturnal dipping pattern are not consistent and independence from 24-hour BP has not often been studied. The dipping pattern and the night–day BP ratio significantly and independently predict mortality and cardiovascular events in hypertensive patients without history of major cardiovascular disease.

Nocturnal BP and cardiovascular risk factors

In the Vilnius University Hospital, we conducted a retrospective study of 103 normotensive young people to determine the relations between nocturnal BP and cardiovascular risk factors.

The aim of our research was to identify the dipping pattern of nocturnal BP and the various dipping categories among normotensive young people (under 35 years old) without CVD to determine the relationship between dipping categories on the one side and CVD risk factors and lifestyle patterns on the other side; and to determine the impact of risk factors on nocturnal BP.

In our retrospective study, we examined 103 normotensive young people without CVD. The 24-hour ABPM was used to estimate nocturnal BP and its dipping pattern. The questionnaire was carried out to determine the patients' life pattern and cardiovascular risk factors.

Of 103 examined patients, 54 (52 %) were men and 49 (48 %) were women. Their mean age was 28.5 years (±4.4 SD). Sixty-six patients (64 %) had normal weight, 24 (23 %) were overweight, and 13 (13 %) were obese. There were18 smokkers (17.5 %), and 49 patients (48 %) were doing sports.

Regarding the dipping categories, 12 patients (12 %) were extreme dippers, 45 (43 %) were dippers, 43 (42 %) were nondippers, and 3 (3 %) were reverse dippers (Table 3).

Table 3. **Characteristics of the study group**

Characteristics	Frequency (%), n=103
Gender	
- Female	48
- Male	52
BMI	
- Normal weight	64
- Overweight	23
- Obese	13
Smoking	
- Smokers	17,5
- Nonsmokers	82,5
Sport	
- No sport activity	52
- Doing sport	48

Table 3 **(continued)**

Characteristics	Frequency (%), n=103
Dipping categories	
- extreme dippers	12
- dippers	43
- 88S&1RB&S	42
- reverse dippers	3

It was estimated that the mean nocturnal BP among men was 10 mmHg higher than among women, obese patients had their mean nocturnal BP higher than patients with normal BMI (127±12/74±6 vs. 104±11/59±8 mmHg; *P* = 0.000, Figure 1 and Figure 2).

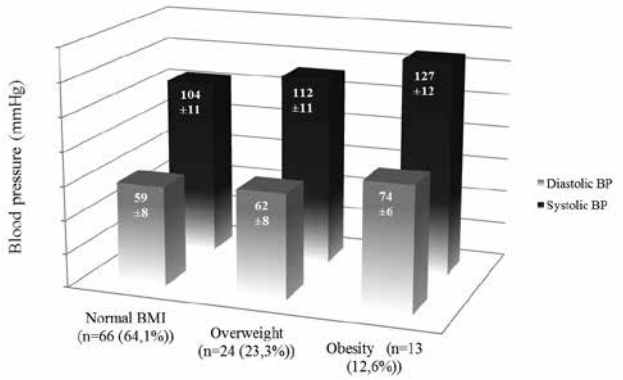

Figure 1. Relationship between the Mean Value of Nocturnal BP and BMI (*P*<0,01)

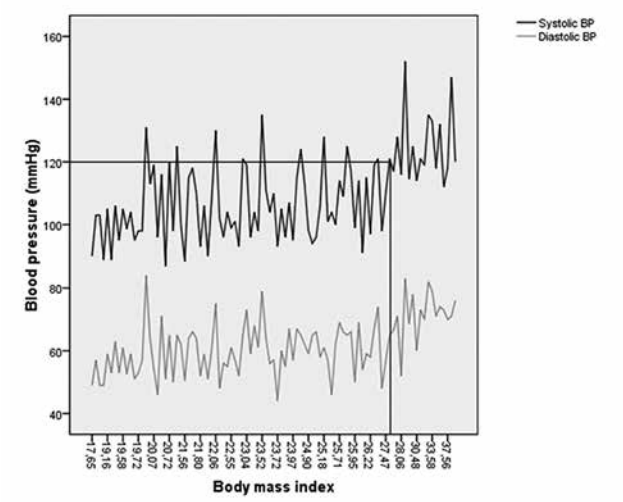

Figure 2. Relationship between the Mean Value of Nocturnal BP and BMI

The nocturnal BP decrease among smokers was lower than among nonsmokers (8±8 vs. 13±6 %; *P*<0.05). On the contrary, sporty patients had a greater digrease (14±6 vs. 10±7 %; *P*=0.03).

Conclusion

The use of ABPM can improve BP monitoring so that treatment can be optimized more rapidly and more patients can achieve BP targets. ABPM increases patient awareness of hypertension management, reduces the overall costs associated with hypertension management, and may improve adherence to drug therapy. Further studies of ABPM may help identify specific predictors of poor prognosis. ABPM may also demonstrate utility in differentiating among, as well as within, classes of antihypertensive agents to determine the most effective agent or regimen for 24-hour BP control. ABPM has been shown to be particularly beneficial in specific populations for predicting target organ damage, identifying masked hypertension, and assessing the risk of cardiovascular events and mortality [4].

Finally, in our retrospective study, it was estimated that there are direct relations between cardiovascular risk factors and the figures of nocturnal BP, dipping categories can be determined by the patients' living pattern. Our findings and further research can increase the efficiency of CVD prevention.

Conflict of interest: None declared

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