Variability of circadian blood pressure profile during 24-hour ambulatory blood pressure monitoring in hypertensive patients

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Abstract

Background: Evaluation of circadian blood pressure (BP) profile is an important element of ambulatory BP monitoring (ABPM). Abnormal nocturnal fall in BP is more common in patients with secondary causes of hypertension and in the elderly. Cardiovascular risk is substantially increased in these patients.

Aim: Analysis of circadian BP profile in a population of treated hypertensives and identification of factors affecting variability of nocturnal fall in BP.

Methods: 24-h ABPM was performed in hypertensive patients. Based on nocturnal fall pattern, four subgroups were identified: dippers, non-dippers, extreme dippers, and risers. Comorbidities were assessed, and data obtained in all groups were compared with the dipper profile group.

Results: We analysed 161 patients (86 men, 53.4%). A dipper profile was noted in 44.7% of patients. Abnormal circadian BP profile was observed in 55.3% of patients, including a non-dipper profile in 21.1% of patients, an extreme dipper profile in 32.3% of patients, and a riser profile in 1.9% of patients. No significant differences in the rates of dyslipidaemia, previous myocardial infarction, previous stroke, and coronary artery disease were seen between the groups. The whole study population was also characterised by similar rates of excessive body weight and abdominal obesity.

Conclusions: An abnormal circadian BP profile was found in over 50% of hypertensive patients. A negative correlation was found between nocturnal BP fall and the patient age. No differences were found between groups with different circadian BP pattern regarding duration of hypertension and the presence of dyslipidaemia, obesity, diabetes, or coronary artery disease.

Key words: hypertension, ambulatory blood pressure monitoring, nocturnal fall

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INTRODUCTION

Evaluation of circadian blood pressure (BP) profile is an important element of 24-h ambulatory BP monitoring (ABPM). Nocturnal fall (NF) may relate to both systolic and diastolic BP. Normal NF range is 10–20%, and these patients are categorised as dippers. It has been estimated that normal circadian BP profile is preserved in about 70% of patients receiving antihypertensive treatment [1]. Abnormal circadian BP profile is seen mostly in patients with secondary forms of hypertension, but also in patients with abnormal metabolic profile and the elderly. Few data are available on factors affecting abnormal circadian BP profile in patients with established hypertension. Identification of such factors may be important in treated hypertensives, as left ventricular hypertrophy, microalbuminuria, vascular remodelling, and atherosclerotic lesions are all seen significantly more frequently in non-dippers compared to dippers [2]. Lack of normal NF is associated with an increased incidence of cardiovascular disease [3]. Knowledge of factors predisposing to abnormal circadian BP profile would allow identification of patients in whom ABPM would be particularly helpful and lead to treatment modifications.

The aim of this study was to evaluate circadian BP profile using ABPM in patients receiving antihypertensive treatment, and to identify factors affecting variability of circadian BP profile in the study population.

METHODS

We studied consecutive outpatients aged 19–85 years who received antihypertensive treatment. For the purpose of this study, a 24-h ABPM was performed in each patient, using the A&D TM 2430 device (Suntech Medical) validated by the European Society of Hypertension [4, 5]. BP was measured by oscillometric method. Sleep and wake periods were reported by patients after the monitoring. Exclusion criteria included arrhythmia precluding successful BP measurements and abnormal sleep-wake cycle (e.g., in night shift workers). Monitoring was initiated in the morning hours on workdays. After the ABPM device was fitted, the patients were advised to return to their usual daily and professional activities. ABPM was continued for at least 24 h. BP measurements were performed every 15 min during a predetermined wake period and every 30 min during the sleep period. Recordings with > 30% of measurement errors were excluded from the analysis. Depending on the size of nocturnal BP fall, patients were categorised into four groups: dippers (NF by 10–20%), non-dippers (NF by 0–10%), extreme dippers (NF by > 20%), and risers/inverse dippers (when no NF in BP was observed or the mean BP was higher during the night compared to the daytime). To account for variability of both systolic and diastolic BP, the size of NF was defined based on mean arterial pressure (MAP) values. We evaluated age, gender, duration of hypertension, obesity, smoking, and history of diabetes, coronary artery disease and dyslipidaemia in patients subgroups defined based on the occurrence and size of NF in ABPM, with dippers as the reference group for comparisons.

Statistical analysis

Statistical analysis was performed using the Student t test and the χ^2 test for nonparametric variables, a correlations between continuous variables were evaluated using the Pearson correlation coefficient. $P < 0.05$ was considered statistically significant. Calculations were performed using the Statistica 8.0 package (Stat Soft Inc., Tulsa, OK, USA).

RESULTS

ABPM was performed in 161 patients, including 86 (53.4%) men. The mean age was 50.7 ± 14 (range 19–85) years. By ABPM, 72 (44.7%) patients were dippers, 34 (21.1%) patients were non-dippers, 52 (32.3%) patients were extreme dippers, and 3 (1.9%) patients were risers (Fig. 1). As the last group was considered to small to be representative, it was excluded from further analyses. Mean nighttime systolic/diastolic BP was 120.86 ± 14/69.02 ± 7.68 mm Hg in dippers, 127.20 ± 14.68/73.44 ± 8.41 mm Hg in non-dippers, and 106.05 ± 12.6/62.55 ± 8.79 mm Hg in extreme dip-
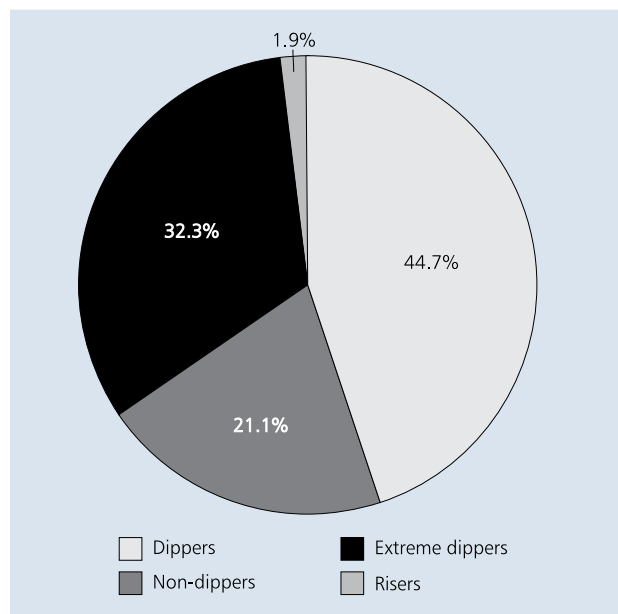

Figure 1. Nocturnal blood pressure fall patterns in the study population

pers. Mean values of both systolic and diastolic BP were abnormal in the dipper and non-dipper groups.

Dyslipidaemia was present in 41 (56.9%) patients in the dipper group, 21 (58.8%) patients in the non-dipper group, and 27 (51.9%) patients in the extreme dipper group, without significant differences between the groups. Type 2 diabetes was present in 9 patients in our study population, including 4 (5.5%) dippers, 2 (5.9%) non-dippers, and 3 (5.7%) extreme dippers. Smoking was reported by 11 (15.3%) patients in the dipper group, 8 (23.5%) patients in the non-dipper group (p = 0.39), and 20 (38.4%) patients in the extreme dipper group (p = 0.0242). No significant differences between groups were found in regard to the history of myocardial infarction, coronary artery disease, and stroke, as well as family history of cardiovascular disease. Abnormal body weight, defined as body mass index ≥ 25.0 kg/m^2, was noted in 46 (63.8%) dippers, 28 (82.3%) non-dippers, and 35 (67.3%) extreme dippers, without significant differences between the groups. Rates of abdominal obesity, defined as waist circumference ≥ 80 cm in women and ≥ 94 cm in men, also did not differ between the groups. Characteristics of the study groups are shown in Table 1. We found a negative correlation between NF in BP and the patient age (r = –0.2368, p = 0.002) in the overall study population (Fig. 2) which was present both in women (r = –0.2939, p = 0.01) (Fig. 3) and men (r = –0.2232, p = 0.039) (Fig. 4).

DISCUSSION

ABPM monitoring is an important tool in the diagnosis of hypertension and to evaluate treatment effectiveness. In addition, conditions such as white coat hypertension, masked

Table 1. Characteristics of the study population

Variable	Nocturnal blood pressure fall pattern			P
	Dippers (n = 72)	Non-dippers (n = 34)	Extreme dippers (n = 52)	
Age [years]	51.1 ± 14.6 (19–79)	53.5 ± 12.7 (28–85)	46.7 ± 12.7 (20–71)	NS[1,2]
Male gender	36 (50%)	20 (58.8%)	28 (53.8%)	NS[1,2]
Duration of hypertension [years]	6.1 ± 7.2 (0–30)	4.9 ± 6.1 (0–25)	3.7 ± 5.0 (0–20)	NS[1,2]
Diabetes	4 (5.5%)	2 (5.9%)	3 (5.7%)	NS[1,2]
Dyslipidaemia	41 (56.9%)	21 (58.8%)	27 (51.9%)	NS[1,2]
Smoking	11 (15.3%)	8 (23.5%)	20 (38.4%)	NS[1]
				p = 0.0242[2]
Abnormal body weight	46 (63.8%)	28 (82.3%)	35 (67.3%)	NS[1,2]
Abdominal obesity	40 (55.6%)	21 (61.8%)	31 (59.6%)	NS[1,2]
History of stroke	5 (6.9%)	2 (5.9%)	0 (0%)	NS[1,2]
Coronary artery disease	8 (11.1%)	3 (8.8%)	2 (3.8%)	NS[1,2]
Family history of CVD	25 (34.7%)	11 (32.4%)	16 (30.8%)	NS[1,2]
Mean decrease in MAP during the night	14.9%	6.57%	24.9%	

[1]Non-dippers vs. dippers; [2]Extreme dippers vs. dippers; CVD — cardiovascular disease; MAP — mean arterial pressure; NS — non-significant
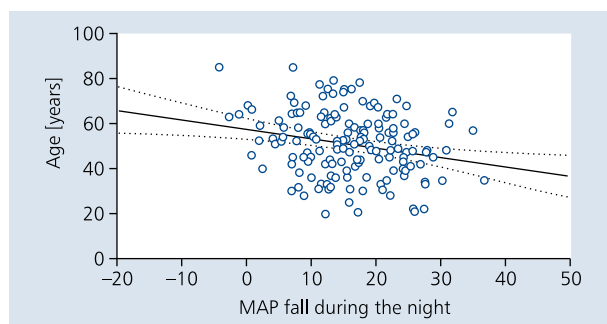

Figure 2. Correlation between nocturnal blood pressure fall and the patient age; MAP — mean arterial pressure
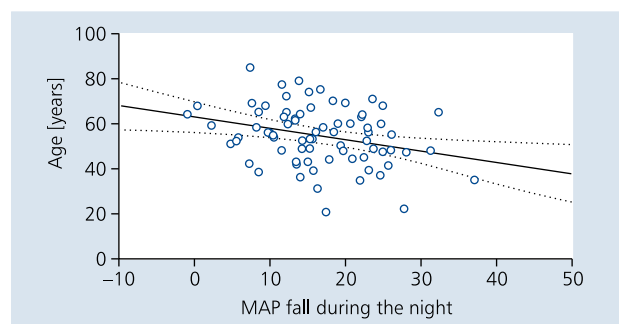

Figure 3. Correlation between nocturnal blood pressure fall and the patient age in women; MAP — mean arterial pressure

Figure 4. Correlation between nocturnal blood pressure fall and the patient age in men; MAP — mean arterial pressure

hypertension, and pseudoresistance to treatment may be identified using ABPM. This method also allows evaluation of the circadian BP profile including such variables as morning surge and NF in BP. As already mentioned, absent NF or NF by < 10% is associated with an increased cardiovascular risk. A non-dipping pattern is more frequently seen in secondary hypertension [6–11]. Abnormally low NF was also noted in type 2 diabetes complicated by neuropathy, autonomic nervous system dysfunction, and obstructive sleep apnoea [12–14]. Our analysis indicates that NF decreases with age, leading to an increased rate of the non-dipping pattern in the elderly. A higher prevalence of the non-dipping pattern in the elderly was also found in the Spanish Society of Hypertension Ambulatory Blood Pressure Monitoring Registry that included 42,947 hypertensives [15]. A higher rate of the non-dipping pattern in the elderly was observed both in treated and untreated subjects. Decreasing NF with age, particularly in patients > 70 years of age, was also reported by Staessen et
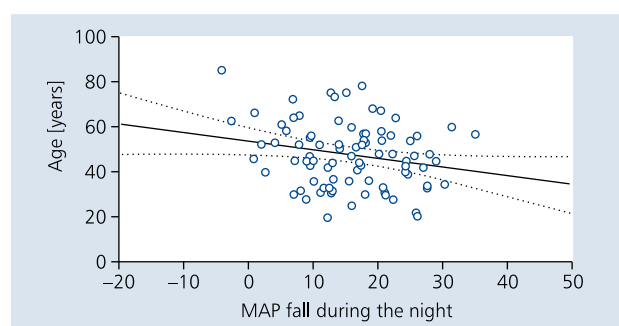
al. [16]. A higher rate of the non-dipping pattern among patients > 50 years of age compared to younger subjects was also found in a population of 9,357 patients what included both hypertensives (41.3%) and normotensives. The non-dipping

pattern was more frequent both among elderly women (31.3% vs. 25.9%) and elderly men (29.7% vs. 25.7%) [17].

Despite widespread use of ABPM in the clinical practice, its findings may be interpreted in different ways, and in some situations this may lead to varying conclusions. Evaluation of nocturnal BP fall is one example of such ambiguity, as NF may be calculated using systolic BP, diastolic BP, or MAP. Thus, the same patient may be categorised differently depending on the method used [18]. In the above mentioned Spanish registry, evaluation of NF was based on systolic BP. In our study, NF was calculated based on MAP and thus reflected both systolic and diastolic BP. One rationale for such an approach is the fact that during exercise, systolic BP increases and diastolic BP decreases, and thus determination of NF based on systolic BP only may lead to some errors in its estimation. In addition, most ABPM devices use the oscillometric method in which MAP is the most reliably estimated BP parameter.

Another issue with ABPM that has been discussed in the literature is the reproducibility of this method. It seems that single ABPM recording is insufficient in this regard. Available evidence indicates that the size of NF may be different in 2 recordings performed in the same patient, regardless of the methodology used, and thus a patient may be categorised as having 2 different NF patterns based on two ABPM recordings. Manning et al. [19] evaluated reproducibility of NF in 2 ABPM recordings performed 6 months apart. A consistent dipper pattern was found during 2 recordings in only 54% of subjects. This study included both normotensives and untreated hypertensives. In another study in 170 patients with hypertension, ABPM was performed twice, 12 months apart [20]. In more than 40% of patients, a difference in NF size was found between the 2 ABPM recordings that resulting in categorisation of patients into 2 different NF categories. In a study that utilized 48-h ABPM, reproducibility of NF was only 75% [21]. On the other hand, the study by Stenehjem et al. [22] indicates that high reproducibility of NF pattern in 2 consecutive ABPM recordings is also possible, as it exceeded 80% in that study. Differences in NF seen in the same person when subjected to more that one ABPM recording may be explained by varying daytime activity. In our study, duration of daytime activity and nighttime rest was reported by the patient, and patients were advised to continue with normal activities. We did not use tools allowing objective evaluation of patient activity using additional devices or sensors. Night shift workers were excluded from the study due to an abnormal sleep and activity pattern resulting in reversed circadian BP profile. Reduced daytime activity, which may also be related to the fact of ABPM recording, may lead to lower daytime BP values and a reduced difference between daytime and nighttime BP. As a result, the patient may be categorised as a non-dipper. In this regard, reliability and reproducibility of ABPM may be increased by objective evaluation of patient activity using appropriate sensors [23, 24]. Reproducibility of

NF in consecutive recordings is also affected by the position of the body during sleep, and the position of the limb with the BP cuff during the measurement. These methods of objective evaluation are not routinely used during ABPM. Serial ABPM recordings might be an alternative approach, leading to collection of more reliable data.

Limitations of the study

Our study had a number of limitations. We performed 24-h ABPM only once which might have resulted in moderately precise determination of NF and circadian BP profile. It might have also been one reason for the observed lack of differences between the study groups. The purpose of our study was to evaluate variability of circadian BP profile based on ABPM, and we did not assess target organ damage or analyse results in relation to the treatment used.

CONCLUSIONS

An abnormal circadian BP profile (non-dipper, extreme dipper, riser) was found in over 50% of hypertensive patients. A negative correlation was found between nocturnal BP fall and the patient age. Variability of circadian BP profile was not affected by duration of hypertension, gender, excess body weight, and the presence of dyslipidaemia, diabetes, or coronary artery disease.

Conflict of interest: *none declared*

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Zmienność dobowego profilu ciśnienia tętniczego u chorych leczonych hipotensyjnie

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Streszczenie

Wstęp: Ocena dobowego profilu ciśnienia tętniczego stanowi istotny element analizy 24-godzinnego monitorowania ciśnienia tętniczego krwi (ABPM). Nieprawidłowości w dobowym profilu ciśnienia tętniczego obserwuje się częściej u pacjentów z wtórnymi przyczynami nadciśnienia tętniczego, wśród chorych z zaburzonym profilem metabolicznym i osób w podeszłym wieku. W grupie tej częściej dochodzi do przerostu mięśnia lewej komory, mikroalbuminurii, przebudowy naczyń i rozwoju zmian miażdżycowych.

Cel: Celem pracy były analiza dobowego profilu ciśnienia tętniczego u chorych z nadciśnieniem tętniczym leczonych hipotensyjnie oraz próba identyfikacji czynników wpływających na jego zmienność w badanej populacji.

Metody: Do badania włączano kolejnych pacjentów z nadciśnieniem tętniczym, leczonych hipotensyjnie. U chorych przeprowadzono ABPM. Wyróżniono 4 podgrupy osób w zależności od wartości nocnego spadku ciśnienia tętniczego: *dipper*, *non-dipper*, *extreme dipper*, *riser*. Przeanalizowano zależność dobowego profilu ciśnienia tętniczego od wieku, płci, czasu trwania nadciśnienia tętniczego, wskaźnika masy ciała, otyłości brzusznej, nikotynizmu, wywiadu: cukrzycy, dyslipidemii, choroby niedokrwiennej serca. Grupę kontrolną stanowili pacjenci o profilu typu *dipper*.

Wyniki: Analizą objęto 161 chorych (86 mężczyzn; 53,4%). Profil typu *dipper* stwierdzono u 44,7% pacjentów. Nieprawidłowy profil ciśnienia tętniczego prezentowało 55,3% badanych: *non-dipper* — 21,1%, *extreme dipper* — 32,3%, *riser* — 1,9% osób. Częstość występowania dyslipidemii wynosiła: *dipper* — 56,9%, *non-dipper* — 58,8%, *extreme dipper* — 51,9% pacjentów. Nie stwierdzono istotnie statystycznych różnic w częstości występowania zaburzeń lipidowych, zawałów serca, choroby wieńcowej, udarów mózgu. Nadmierną masę ciała zaobserwowano u 63,8% chorych typu *dipper*, u 82,3% — *non-dipper* i 67,3% — *extreme dipper*. Nie zanotowano różnic w występowaniu nadmiernej masy ciała ani otyłości brzusznej między badanymi podgrupami chorych.

Wnioski: W badanej populacji ponad połowa pacjentów z nadciśnieniem tętniczym charakteryzowała się nieprawidłowym profilem ciśnienia tętniczego. Istnieje korelacja między wiekiem chorego a zmniejszaniem się nocnego spadku ciśnienia tętniczego. Nie stwierdzono różnic w zakresie czasu trwania nadciśnienia tętniczego, częstości występowania nadwagi i otyłości, hiperlipidemii, cukrzycy, choroby niedokrwiennej serca między pacjentami o różnym profilu nocnego spadku ciśnienia tętniczego.

Słowa kluczowe: nadciśnienie tętnicze, ABPM, nocny spadek

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