Cardiovascular Ultrasound

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Non-dipper treated hypertensive patients do not have increased cardiac structural alterations

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Published: 14 February 2003

Cardiovascular Ultrasound 2003, **1**:1

Received: 27 January 2003
Accepted: 14 February 2003

This article is available from: http://www.cardiovascularultrasound.com/content/1/1/1

Abstract

Background: Non-dipping pattern in hypertensive patients has been shown to be associated with an excess of target organ damage and with an adverse outcome. The aim of our study was to assess whether a reduced nocturnal fall in blood pressure (BP), established on the basis of a single 24-h BP monitoring, in treated essential hypertensives is related to more prominent cardiac alterations.

Methods: We enrrolled 229 treated hypertensive patients attending the out-patient clinic of our hypertension centre; each patient was subjected to the following procedures : 1) clinic BP measurement; 2) blood and urine sampling for routine blood chemistry and urine examination; 3) standard 12-lead electrocardiogram; 4) echocardiography; 5) ambulatory BP monitoring (ABPM). For the purpose of this study ABPM was carried-out in three subgroups with different clinic BP profile : 1) patients with satisfactory BP control (BP < 140/90 mmHg; group I, n = 58); 2) patients with uncontrolled clinic BP (clinic BP values ≥ 140 and/or 90 mmHg) but lower self-measured BP (< 20 mmHg for systolic BP and/or 10 mmHg for diastolic BP; group II, n = 72); 3) patients with refractory hypertension, selected according to WHO/ISH guidelines definition (group III, n = 99). Left ventricular hypertrophy (LVH) was defined by two gender-specific criteria (LV mass index ≥125/ m^2 in men and 110 g/m^2 in women, ≥51/$gm^{2.7}$ in men and 47/g/$m^{2.7}$ in women).

Results: Of the 229 study participants 119 (51.9%) showed a fall in SBP/DBP < 10% during the night (non-dippers). The prevalence of non-dippers was significantly lower in group I (44.8%) and II (41.6%) than in group III (63.9%, p < 0.01 III vs II and I). The prevalence of LVH varied from 10.3 to 24.1% in group I, 31.9 to 43.1% in group II and from 60.6 to 67.7% in group III (p < 0.01, III vs II and I). No differences in cardiac structure, analysed as continuous variable as well as prevalence of LVH, were found in relationship to dipping or non-dipping status in the three groups.

Conclusions: In treated essential hypertensives with or without BP control the extent of nocturnal BP decrease is not associated with an increase in LV mass or LVH prevalence; therefore, the non-dipping profile, diagnosed on the basis of a single ABPM, does not identify hypertensive patients with greater cardiac damage.

Background

Left ventricular hypertrophy (LVH) established either by electrocardiography or echocardiography is an important predictor of cardiovascular morbidity and mortality in the general population, in hypertensive patients and in patients with coronary artery disease [1–4]. Although LVH in hypertensive patients is an adaptive response to increased left ventricular wall stress, the development of myocardial hypertrophy is dependent on several hemodynamic and humoral factors. Duration and severity of hypertension, diurnal variations of blood pressure (BP), and 24 hour overall BP variability are the most important hemodynamic variables involved in the pathogenesis of LVH [5,6]. The advent and the large diffusion of non-invasive techniques for measuring ambulatory BP have made it possible to monitor BP throughout the day. The prevalent circadian pattern in both normotensive and hypertensive individuals is characterized by a marked decrease of systolic and diastolic BP during the night (dippers), but there is a noticeable fraction of subjects who exhibit a diminished nocturnal decline in BP (non-dippers) [7,8]. Many clinical studies with non-invasive ambulatory BP monitoring (ABPM) have shown that some cardiovascular complications of arterial hypertension and namely LVH, tend to be more frequent in patients in whom BP does not fall, or falls scarcely at night and consequently, suffer a prolonged exposure to high BP lever over the 24 hour [9–11]. Moreover, three prospective studies conducted in patients with hypertension [12–14] and one population-based longitudinal survey confirmed that a reduced nocturnal decline in BP is a predictor of cardiovascular events [15]. However, the clinical significance of the non-dipping pattern has not gone undisputed. Some recent studies have not shown substantial differences between the extent of cardiovascular preclinical alterations among untreated hypertensive dippers and non-dippers with similar BP load throughout the 24 hour period [16,17]. Furthermore, it has been demonstrated that the classification of hypertensive patients into dippers and non-dippers based on single ABPM has a poor reproducibility over time, both in the absence and the presence of treatment [18,19].

In this study we have evaluated, in a large group of treated essential hypertensive patients, with different clinic BP patterns, whether the extent of nocturnal fall in BP, assessed on the basis of a single 24 hour ABPM, is related to left ventricular alterations.

Methods

Patients and design

The present analysis involved 229 patients with treated essential hypertension attending the out-patient clinic of our hypertension centre during a period of nine months (2 january – 30 september 2001). One hundred twenty five out of 229 patients had been referred to our centre for the first time by their general practitioners because of inadequate BP control or in order to exclude secondary forms of hypertension and the remaining 104 patients had been regularly followed-up (one or two times/year, mean 1.3) for a period of at least six months (range 6–122). Three subgroups of subjects with different clinic BP profile were selected for the aim of this study : 1) patients with satisfactory clinic BP control (clinic BP values < 140/90 mmHg) (group I, n = 58); 2) patients with uncontrolled clinic BP (clinic BP values ≥ 140 and/or ≥ 90 mmHg) but lower self-measured BP (< 10 mmHg for diastolic BP and/or < 20 mmHg for systolic BP; group II, n = 72); 3) patients with refractory hypertension (persistent clinic BP values of 140/90 mmHg or above, or as persisting systolic BP values of 140 mmHg or above in the case of isolated systolic hypertension, despite the assumption of three or more antihypertensive drugs in adequate doses in the past three months) (group III, n = 99) [20]. After informed consent had been obtained during the initial or follow-up visit all patients were subjected to the following procedures within 1–3 weeks : 1) clinic BP measurement ; 2) blood and urine sampling for routine blood chemistry and urine examination; 3) standard 12-lead electrocardiogram; 4) echocardiogram; 5) ambulatory BP monitoring. In all subjects special laboratory studies for secondary causes of hypertension were performed when considered appropriate on clinical grounds. Patients with secondary hypertension, congestive heart failure, previuos myocardial infarction, cardiac valve diseases, history of coronary artery by-pass, poor echocardiographic window, conditions preventing technically adequate ABPM (e.g. atrial fibrillation and other major dysrhythmias) and major non-cardiovascular disease were excluded. Compliance to treatment was evaluated systematically during patient's visits by structured questions on the regularity of drug consumption.

Clinic blood pressure measurement

BP was measured in the hospital out-patient clinic by a physician with a mercury sphygmomanometer (first and fifth phases of Koroktoff sounds taken as SBP and DBP respectively) after the subjects had rested for 5–10 min in the sitting position. Three measurements were taken at 1 min intervals, and the average was used to define clinic systolic and diastolic BP.

Ambulatory blood pressure monitoring

Twenty-four-hour ABPM was carried out on the non-dominant arm using a Spacelabs 90207 device (Spacelabs Inc., Richmond, Washington, USA) after validation of readings against a mercury sphygmomanometer by means of a Y tube. The device was set to obtain BP readings at 15 min intervals during the day (0700–2300 h) and at 20 min intervals during the night (2300–0700 h). The time of application (± 1 h) and the type of device were the same in all

Table 1: Clinical and laboratory characteristics of study population

	I (n = 58)	II (n = 72)	III (n = 99)	P
Age (years)	54.1 ± 8.5	56.1 ± 10.1	56.6 ± 12.2	NS
Gender (M/F)	32/26	47/25	47/52	NS
Body mass index (kg/m^2)	25.6 ± 3.2	26.1 ± 3.1	28.4 ± 5.1	p <0.01*
Duration of HT (years)	6.9 ± 5.1	6.3 ± 4.9	7.1 ± 5.0	NS
Current smokers (%)	25.9	24.2	26.5	NS
Heart rate (b/min)	72.3 ± 8.1	72.5 ± 12.1	69.9 ± 10.1	NS
		Clinic BP:		
SBP (mmHg)	128.4 ± 13.2	157.9 ± 14.9	164.4 ± 23.0	p < 0.01*
DBP (mmHg)	81.1 ± 7.0	97.4 ± 8.4	98.3 ± 11.3	p < 0.01§
		Ambulatory BP		
24-h SBP(mmHg)	125.3 ± 8.6	131.1 ± 11.3	144.1 ± 16.8	p < 0.01*
24-h DBP(mmHg)	80.0 ± 6.0	80.6 ± 8.3	85.6 ± 11.8	p < 0.01*
Daytime SBP(mmHg)	129.0 ± 9.6	136.3 ± 11.6	147.3 ± 17.9	p < 0.01*
Daytime DBP(mmHg)	83.5 ± 6.8	85.4 ± 8.6	89.8 ± 11.5	p < 0.05 *
Nighttime SBP (mmHg)	115 ± 8.8	120.7 ± 12.9	135.5 ± 18.7	p < 0.01*
Nighttime DBP (mmHg)	70.8 ± 6.1	71.5 ± 9.3	77.8 ± 10.6	p < 0.01*
Blood glucose(mmol/l)	5.17 ± 0.67	5.44 ± 0.96	5.80 ± 1.72	p < 0.05§
T serum cholesterol (mmol/l)	5.73 ± 0.93	5.84 ± 0.96	5.71 ± 1.07	NS
Serum creatinine(μmol/l)	88.1 ± 16.2	89.2 ± 15.6	88.2 ± 22.6	NS

Data are means ± SD; NS = not significant; HT = hypertension; SBP = systolic blood pressure ; DBP = diastolic blood pressure * III vs II, I ; §III vs I ;

patients. The patients were instructed to attend their usual day-to-day activities but to keep still at the times of measurements ; all subjects were asked to go to bed not later than 2300 h and to stay in bed until 0700. The BP monitoring was always performed over a working day (Monday to Friday). Each ABPM dataset was first automatically scanned to remove artefactual readings, according to preselected editing criteria. Systolic readings > 260 or < 70 mmHg and diastolic readings > 150 or < 40 mmHg were automatically discarded. The recording was then analysed to obtain 24 h, daytime and night-time average SBP, DBP and heart rates. Nocturnal dipping was defined as a reduction in average SBP and DBP at night greater than 10% compared with average daytime values [10].

Echocardiography

M-mode, two-dimensional and Doppler echocardiographic examinations were performed with subjects in the partial left decubitus position using commercially available instruments (ATL HDI 3000 and 5000, Bothell, Washington, USA) equipped with 2.25 or 2.5 MHz imaging transducers. End-diastolic and end-systolic left ventricular internal diameter (LVIDd, LVIDs), interventricular septum thickness (IVST) and posterior wall thickness (PWT) were calculated from two-dimensionally guided M-mode tracing and measured during five consecutive cycles according to the Penn convention [21]. Left ventricular mass was estimated by Devereux's formula and normalized by body surface area or height $^{2.7}$ [22,23]. Relative wall thickness (RWT) was calculated as (2xPWT/LVIDd). LVH was defined following two different criteria, i.e. when left ventricular mass index (LVMI) was equal or exceeded 125 g/m^2 in men and 110 g/m^2 in women (24), and 51 g/m$^{2.7}$ in men and 47 g/m$^{2.7}$ in women [25]. Patterns of left ventricular geometry were defined according to Ganau et al. [26] : 1) LV concentric remodelling, when a normal LVMI was combined with RWT ≥ 0.45; 2) concentric LVH, when left ventricular hypertrophy occurred with a RWT ≥ 0.45; 3) eccentric LVH, when increased LV mass was associated with RWT < 0.45. Left ventricular systolic function was assessed by endocardial fractional shortening. Left ventricular filling was assessed by recording mitral flow by standard pulsed Doppler technique, and the following parameters were considered : early diastolic peak flow velocity (E), late diastolic peak flow velocity (A) and the ratio of the early to late flow velocity peaks (E/A ratio).

Statistical analysis

Values have been expressed as means ± SD or as percentages. Differences between groups were assessed by analysis of variance (ANOVA) with the Scheffe post-hoc test. Mean values for dipper and non-dipper patients were compared using Student's t-test for independent samples. Chi-square statistics were used to compare categorical variables between groups. Correlations were obtained by using Pearson's equation. The limit of statistical significance was set at P < 0.05. Data management and statistical anal-

Table 2: Anti-hypertensive medications of study population

	Group I	Group II	Group III	P
Diuretics	52 %	42%	78%	p < 0.01*
ACE inhibitors and Angiotensin II antagonists	65%	66%	86%	p < 0.01*
Calcium Antagonists	41%	47%	67%	p < 0.05*
Beta-blockers	29%	41%	57%	p < 0.05*
Alpha-blockers	3%	7%	31%	p < 0.05*
		Treatment regimens		
	Group I	**Group II**	**Group III**	**P**
Monotherapy	28%	37%	0%	p < 0.01*
Two drugs	55%	30%	0%	p < 0.01*
Three drugs	14%	21%	51%	p < 0.01*
Four or more drugs	3%	12%	49%	p < 0.01*

* III vs II and I

ysis were performed using Statwiev SAS Version 4.5 Software (Abacus Concepts Inc, Berkeley, USA).

Results

Demographic, clinical and laboratory characteristics of the study population are reported in Table 1. Mean age, heart rate, known duration of hypertension, smoking habit, creatinine, total serum cholesterol did not differ significantly between the groups. Body mass index, clinic SBP and ambulatory SBP/DBP were significantly higher in patients with refractory hypertension than in other two groups. Serum glucose and DBP were significantly greater in group III than in group I. Pharmacological treatment regimens were substantially different in the three groups (Table 2). 55% of the patients in group I, and 52% in group II were receiving only morning antihypertensive medication ;whereas in almost all refractory hypertensives drugs were administered both at morning and at evening. The compliance with pharmacological treatment was satisfactory in all groups: all patients reported taking the prescribed drugs regularly.

Of the 229 study participants 110 showed a fall in SBP/DBP > 10% during nighttime sleep and were categorized as dippers, while the remaining 119 showed a fall ≤ 10% and were categorized as non-dippers. The prevalence rates of non-dippers were significantly lower in group I (44.8%) and II (41.6%) than in group III (63.9%, $p < 0.01$).

Depending on the method of LV mass indexation and the criteria used, LVH was present in a percentage ranging from 10.3% to 24.1% in group I, 31.9% to 43.1% in group II and from 60.6% to 67.7% in group III. In all three groups a lower prevalence was found using the gender specific partition value indexed by body surface area (125/110 g/m^2). Regardless of the criteria used for the diagnosis eccentric hypertrophy was the most common type of LVH in both group I and II, whereas concentric hypertrophy was the most frequent one in group III.

BP nocturnal profile and cardiac structure and function

Clinical and laboratory characteristics of all three groups according to classification into dippers and non dippers are reported in Table 3, 4 and 5. Left ventricular diastolic and systolic diameter, LV absolute wall ticknessess, as well relative wall thickness, LV mass and LV mass indexed both for body surface area and height $^{2.7}$, endocardial fractional shortening and early/late mitral flow velocity ratio were similar in dippers and nondippers. Moreover, when the echocardiographic data were analysed in a categorical way as presence of absence of cardiac hypertrophy, the prevalence of LVH was similar in all three groups of dippers and nondippers (Fig. 1).

Correlations between LV mass and BP

LVMI did not significantly correlate with any measure of clinic BP or ABP in both group I and II. In contrast in refractory hypertensives (group III) a significant correlation was found only between LVMI and systolic and diastolic daytime BP ($r = 0.21$, $p < 0.03$ and $r = 0.22$, $p < 0.02$); in fact, the strengths of association of LVMI with nighttime BP or 24 hour BP did not attain a statistical significance.

Discussion

The present study carried out in a large sample of treated dipper and non-dipper essential hypertensive patients with different clinic BP control and prevalence of LVH shows that a reduced nocturnal fall in BP, established on the basis of a single ABPM, is not associated with more pronounced cardiac involvement. In fact, we found no difference in left ventricular size, systolic and diastolic

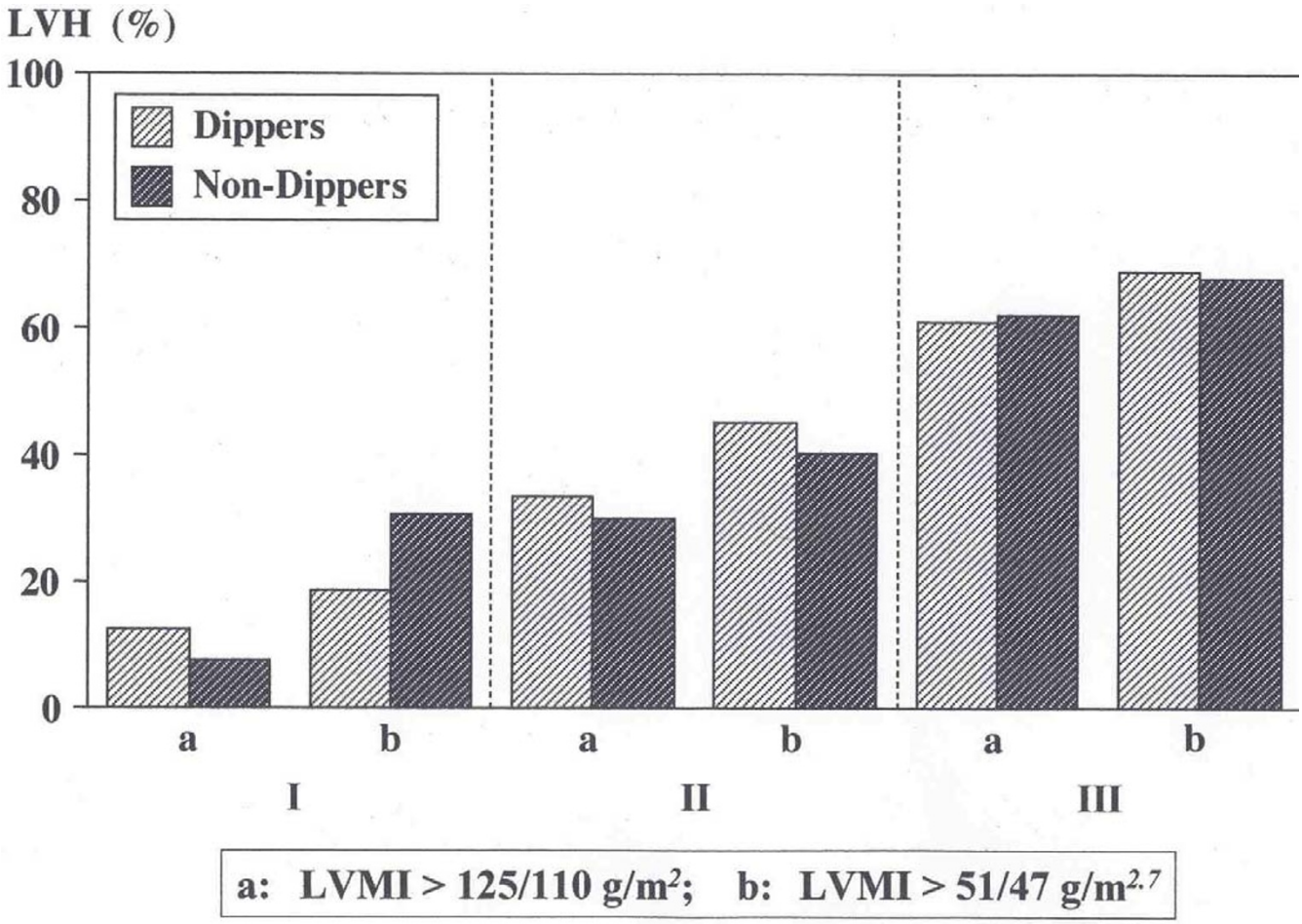

Figure 1
Prevalence of left ventricular hypertrophy (LVH) according two echocardiographic diagnostic criteria in dipper and non-dipper treated hypertensive patients, with different clinic blood pressure profiles : group I (satisfactory clinic BP control), group II (uncontrolled clinic BP, but lower self-measured BP), group III (refractory hypertension).

function or prevalence of cardiac hypertrophy between patients with and without a normal fall in BP during nighttime. This lack of difference in cardiac involvement was found when all three subgroups of dippers and non-dippers were considered, at any level of BP control achieved during chronic antihypertensive therapy. This evidence can be discussed as follows: first, not only the demographic and metabolic characteristics, but also clinic BP and mean 24-h BP values were superimposable in dippers and non-dippers, allowing a comparison between homogenous groups of treated hypertensives that differ only by the extent of nocturnal dip. Therefore, overall 24-h BP load rather than the day-night difference in BP seems to play a pivotal role in the maintenance or regression of LVH in chronically treated hypertensives. It has already been noted that the greater left ventricular mass reported in some studies in non-dippers may not be related to the non-dipping phenomenon per se, but to a greater BP level over 24-h [27]; this may be also true for other signs of target organ damage such as carotid structural alterations [28]. The association between non-dipping and target organ damage, however, remains somewhat controversial. Our data are in agreement with several studies who failed to detect any significant difference between dipper and non-dipper hypertensive patients or found only a very mild impact of a blunted nocturnal BP reduction on cardiovascular characteristics [17,29–31]. In particular, Ferrrara et al. assessing LV structure and diastolic function as well carotid artery morphology in 123 patients with long-standing hypertension in whom antihypertensive treatment was discontinued for a period of 4 weeks, demonstrated any significant difference in LV and carotid

Table 3: Clinical characteristics of patients with satisfactory BP control (group I), according to dipping status.

	Dippers (n = 32)	Non-dippers (n = 26)	P
Age (years)	54.7 ± 8.6	53.4 ± 8.5	NS
Gender (M/F)	17/15	15/11	NS
Body mass index (kg/m^2)	25.2 ± 3.3	26.3 ± 3.2	NS
Duration of HT (years)	6.8 ± 5.6	6.9 ± 5.7	NS
Current smokers (%)	22	30	NS
Heart rate (b/min)	72.1 ± 8.1	74.1 ± 7.5	NS
	Clinic BP		
SBP (mmHg)	123.1 ± 9.3	121.5 ± 10.3	NS
DBP (mmHg)	78.6 ± 7.0	77.6 ± 5.7	NS
	Ambulatory BP		
24-h SBP (mmHg)	127.1 ± 9.7	123.2 ± 6.7	NS
24-h DBP (mmHg)	81.1 ± 6.4	78.7 ± 5.5	NS
Daytime SBP (mmHg)	132.4 ± 10.5	124.9 ± 6.7	$p < 0.01$
Daytime DBP (mmHg)	85.0 ± 6.9	81.0 ± 5.8	$p < 0.05$
Nighttime SBP (mmHg)	112.8 ± 8.9	118.4 ± 7.7	$p < 0.05$
Nighttime DBP (mmHg)	69.3 ± 5.9	72.6 ± 6.0	$p < 0.05$
Blood glucose (mmol/l)	5.15 ± 0.77	5.14 ± 0.49	NS
T serum cholesterol (mmol/l)	5.70 ± 1.01	5.83 ± 0.85	NS
Serum creatinine (μmol/l)	91.3 ± 15.9	86.2 ± 16.5	NS
LVM (g)	171.9 ± 44.0	179.2 ± 37.1	NS
LVMI (g/m^2)	97.0 ± 19.4	98.5 ± 15.9	NS
LVMI (g/m$^{2.7}$)	43.1 ± 8.2	44.6 ± 7.7	NS
RWT	0.40 ± 0.04	0.39 ± 0.07	NS
SF (%)	39.1 ± 5.9	38.7 ± 6.1	NS
E/A	1.3 ± 0.3	1.3 ± 0.4	NS

LVMI = left ventricular mass index; RWT = relative wall thickness; SF = shortening fraction; E/A = early diastolic peak flow velocity (E)/late diastolic peak flow velocity (A). *III vs II e I

structure among dippers and non-dippers, suggesting that unfavorable consequences of non dipper status might be blunted by the duration of hypertension [32]. Second, only in patients with refractory hypertension a significant association between BP levels under treatment and left ventricular mass was found; however, the strengths of these correlations attained a statistical significance for systolic and diastolic daytime BPs but not for nighttime BPs, suggesting a limited effect of nocturnal BP profile, assessed by a single ABPM, on cardiovascular remodelling in this particularly selected group of treated hypertensives. Our results, however, do not demonstrate that the nocturnal BP behavior is not determinant in the development and progression of cardiac structural alterations, but that it is probably not relevant when the nighttime fall in BP has been evaluated on the basis of a single ABPM. The classification of hypertensive patients into dippers and non-dippers has a low reproducibility over time [33,34]. This limited reproducibility is presumably related to the fact that the quality and depth of sleep as well the mental and physical activity during daytime can easily vary from one recording session to another. Omboni et al have shown that about 40% of hypertensive patients included in the Study on Ambulatory Monitoring of Pressure and Lisinopril Evaluation (SAMPLE) classified into dippers and non-dippers changed status when they were studied again after 1 year [19]. Furthermore, the regression of LVH by antihypertensive treatment was significantly due to the therapy-induced decrease in mean 24-h, daytime and nigthttime BP but not to the effect of the day-night difference in BP [35]. Manning et al examined the long-term variability in nocturnal BP pattern and showed that 56% of their subjects did not change the dipping status whereas the remaining 44% had a variable pattern [36]. More recently, ourselves found a different short-term variability in circadian BP according to dipping status at baseline, being significantly greater in patients classified at first ABPM as non-dippers (28%) than in dippers (9%) [36]. Accordingly to these findings the assumption that one single 24-h recording can characterize an individual's habitual nocturnal BP profile needs to be reconsidered. The increasing evidence for the linited reproducibility of circadian variation in BP suggests that in a noticeable proportion of patients the non-dipping pattern cannot be considered as a definite clinical trait. Thirdly, the reduced nocturnal fall in BP was found in the majority of the whole study population (53%), and appeared particularly high in the group of refractory hypertensives (67%) confirming earlier re-

Table 4: Clinical characteristics of patients with uncontrolled clinic BP (group II), according to dipping status.

	Dippers (n = 42)	Nondippers (n = 30)	P
Age (years)	55.7 ± 10.7	56.7 ± 9.3	NS
Gender (M/F)	27/15	20/10	NS
Body mass index (kg/m2)	25.4 ± 2.9	26.5 ± 2.6	NS
Duration of HT (years)	6.1 ± 5.0	6.6 ± 4.9	NS
Current smokers (%)	26.1	29.3	NS
Heart rate (b/min)	73.40 ± 12.25	71.27 ± 12.04	NS
	Clinic BP		
SBP (mmHg)	157.3 ± 14.7	158.8 ± 15.3	NS
DBP (mmHg)	95.6 ± 7.6	97.1 ± 8.9	NS
	Ambulatory BP		
24-h SBP (mmHg)	130.7 ± 10.7	131.7 ± 12.3	NS
24-h DBP (mmHg)	79.9 ± 8.7	81.5 ± 7.8	NS
Daytime SBP (mmHg)	137.4 ± 11.1	134.7 ± 12.3	NS
Daytime DBP (mmHg)	85.4 ± 9.1	85.3 ± 7.9	NS
Nighttime SBP (mmHg)	116.4 ± 11.0	126.7 ± 12.9	0.01
Nighttime DBP (mmHg)	68.5 ± 8.3	75.4 ± 9.2	0.01
Blood glucose (mmol/l)	5.4 ± 0.73	5.5 ± 0.81	NS
T serum cholesterol (mmol/l)	5.77 ± 0.71	5.92 ± 1.21	NS
LVM (g)	196.8 ± 41.6	214.5 ± 61.5	NS
LVMI (g/m^2)	109.3 ± 19.8	113.5 ± 29.6	NS
LVMI ($g/m^{2.7}$)	49.1 ± 9.9	50.6 ± 13.2	NS
RWT	0.42 ± 0.05	0.43 ± 0.05	NS
SF (%)	40.1 ± 7.1	39.3 ± 6.7	NS
E/A	1.4 ± 0.4	1.3 ± 0.5	NS

ports of an increased prevalence of non-dippers among patients receiving antihypertensive therapy compared to untreated patients with recently diagnosed hypertension [38,39]. Different factors may explain this finding : 1) in treated hypertensive patients non-dipping could be associated with the lack of therapeutical coverage for the 24 h of the day; this should be true for group I and II in whom the percentage of patients who were receiving only morning medication was significantly greater among non-dippers as compared with dippers, but probably not for refractory hypertensives (group III), who were taking three or more drugs (scheduled both at morning and at evening); 2) the mechanism(s) involved in the lack of nocturnal dip remains unclear; this complex phenomenon may reflect a predominance of pressure influences (i.e. angiotensin II, chatecolamines etc) over depressor ones (i.e. reduction of sympathetic nerve activity, an increase in vagal activity etc) that help to regulate BP at night, and may also result from structural vascular alterations interfering with resistence vessel dilation [40]. In this context, refractory hypertension may be considered a clinical conditions with a large prevalence of cardiovascular structural alterations [41] potentially responsible for the reduced nocturnal hypotension. However, despite the very high prevalence rates of LVH and non-dipping profile found in our group of refractory hypertensives we failed to demonstrate any difference in cardiac structural and functional abnormalities among dipper and non dipper patients.

Conclusions

The present study performed in treated hypertensive patients with different clinic BP control profiles indicates that the lack of nocturnal decline in BP is not associated with a more pronounced cardiac involvement; these results strengthen the doubts about its clinical significance as an independent risk factor in non-dipper patients classified on the basis of a single 24-h ambulatory BP monitoring.

Competing interests

None declared.

Authors' Contributions

CC : conceived of the study and partecipated in its design and coordination and prepared the manuscript

IM : performed the statistical analysis

SM : carried out the ABPMs, echocardiographic examinations and performed statistical analysis

CV : was involved in the selection of the study population, carried-out echocardiographic examinations

Table 5: Clinical characteristics of patients with refractory hypertension (group III), according to dipping status.

	Dippers (n= 36)	Nondippers (n= 63)	P
Age (years)	53.8 ± 13.5	57.8 ± 11.4	NS
Gender (M/F)	24/12	23/40	NS
Body mass index (kg/m2)	28.5 ± 3.6	27.6 ± 4.9	NS
Duration of HT (years)	7.2 ± 5.4	7.1 ± 5.2	NS
Current smokers (%)	29.9	22.1	NS
Heart rate (b/min)	71.5 ± 10.4	69.2 ± 10.9	NS
	Clinic BP		
SBP (mmHg)	160.1 ± 22.0	165.9 ± 23.6	NS
DBP (mmHg)	99.9 ± 11.2	97.0 ± 11.4	NS
	Ambulatory BP		
24-h SBP (mmHg)	142.5 ± 14.6	144.9 ± 18.0	NS
24-h DBP (mmHg)	88.2 ± 10.3	84.2 ± 12.4	NS
Daytime SBP (mmHg)	149.0 ± 15.2	146.3 ± 19.4	NS
Daytime DBP (mmHg)	93.6 ± 11.0	87.6 ± 11.1	0.05
Nighttime SBP (mmHg)	126.7 ± 13.4	140.4 ± 19.4	0.001
Nighttime DBP (mmHg)	74.2 ± 9.0	79.8 ± 10.8	0.05
Blood glucose (mmol/l)	5.37 ± 0.66	5.97 ± 2.03	NS
T serum cholesterol (mmol/l)	5.83 ± 1.09	5.63 ± 0.95	NS
Serum creatinine (μmol/l)	95.01 ± 21.02	87.76 ± 24.30	NS
LVM (g)	249.5 ± 84.6	228.7 ± 74.6	NS
LVMI (g/m^2)	130.6 ± 37.8	126.6 ± 33.7	NS
LVMI ($g/m^{2.7}$)	61.2 ± 17.4	58.4 ± 17.5	NS
RWT	0.43 ± 0.06	0.45 ± 0.08	NS
SF (%)	38.4 ± 7.4	38.2 ± 7.9	NS
E/A	1.0 ± 0.3	1.1 ± 0.2	NS

GB : was also involved in the selection of the study population

FB : carried out echocardiographic examinations

AZ : partecipated in the design of the study

All authors read and approved the final manuscript

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