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Nocturnal blood pressure in untreated essential hypertensives

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Abstract

Aim. Prevalence, correlates and reproducibility of nocturnal hypertension (NH) as defined by fixed cut-off limits in uncomplicated essential hypertension are poorly defined. Therefore, we assessed such issue in a cohort of 658 untreated hypertensives. *Methods.* All subjects underwent procedures including cardiac and carotid ultrasonography, 24-h urine collection for microalbuminuria, ambulatory blood pressure monitoring (ABPM), over two 24-h periods within 4 weeks. NH was defined according to current guidelines (i.e. night-time blood pressure, BP $\geq$ 120/70 mmHg) and non-dipping status as a reduction in average systolic (SBP) and diastolic BP (DBP) at night lower than 10% compared with daytime values. *Results.* A total of 477 subjects showed NH during the first and second ABPM period; 62 subjects had normal nocturnal BP (NN) in both ABPM sessions. Finally, 119 subjects changed their pattern from one ABPM session to the other. Overall, 72.5% of subjects had reproducible NH, 18% variable pattern (VP) and 9.5% reproducible NN. In the same group, figures of reproducible non-dipping, variable dipping and reproducible dipping pattern were 24%, 24% and 52%, respectively. Among NH patients, 56% of whom were dippers, subclinical cardiac organ damage was more pronounced than in their NN counterparts. *Conclusions.* In uncomplicated essential hypertensives, NH is a more frequent pattern than non-dipping; NH is associated with organ damage, independently of dipping/non-dipping status. This suggests that options aimed at restoring a blunted nocturnal BP fall may be insufficient to prevent cardiovascular complications unless night-time BP values are fully normalized

Key Words: *nocturnal hypertension, non-dipping, organ damage*

Introduction

Cross-sectional and longitudinal studies in hypertensive cohorts and populations support the view that a blunted reduction in blood pressure (BP) at night is associated with conventional cardiovascular (CV) risk factors (1), preclinical target organ damage (2–5) and, more importantly, with an increased incidence of CV events (6–9). In clinical practice and research settings, patients are conventionally categorized according to the circadian BP pattern in dippers and non-dippers (i.e. night to day BP ratio < 0.90 and ≥ 0.90, respectively); this classification was coined by O'Brien and co-workers (10) more than two decades ago.

The dipping status has been regarded as a clinical trait associated to a more favourable prognosis and requiring a less aggressive therapeutic approach compared with the non-dipping profile. This conclusion, however, has been questioned for several reasons. A number of studies have failed to demonstrate substantial differences in surrogate (11–13) and hard end-points between dippers and non-dippers (14–16). Observations in elderly have shown that marked reductions in night-time BP in extreme dippers (i.e. night-day ratio < 0.80) are related to an excess of silent cerebrovascular damage as assessed by magnetic resonance imaging (17,18). A fully preserved BP fall at night in hypertensive subjects may not result in a normal night-time BP profile. In fact, nocturnal hypertension (NH; i.e. average night-time BP $\geq$ 120/70 mmHg) may occur independently from the dipping status; this condition has been shown to

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be associated with vascular and cardiac alterations and with an adverse prognosis regardless daytime BP values (19,20).

As a few studies have investigated the prevalence and correlates of NH, defined by the aforementioned cut-off limits, we addressed this important issue in a large cohort of untreated essential hypertensives.

Methods

Study population

A total of 658 consecutive, never-treated hypertensive subjects referred to our outpatient clinic were included in the study. The analysis was performed on data from the Ambulatory Blood pressure and Organ Damage in Hypertension (ABODH) study, a cross-sectional observational registry targeting the relationship between circadian BP variations and hypertension-related organ damage in untreated subjects with recently diagnosed essential hypertension. Details of the study have been previously published (21).

Briefly, based on history, physical and laboratory examinations, subjects were characterized as having: (i) grade 1 or 2 hypertension (22), diagnosed in the previous 12 months and confirmed during two visits at the outpatient clinic; (ii) no clinically overt CV disease, secondary causes of hypertension, type 1 and 2 diabetes mellitus, renal insufficiency and life-threatening conditions; (iii) no conditions preventing technically adequate ABPM (e.g. atrial fibrillation and major arrhythmias); (iv) no history, symptoms or clinical evidence of sleep apnea syndrome based on the Berlin Questionnaire (23).

After an informed written consent had been obtained, all subjects underwent the following procedures: medical history and physical examination, clinic BP measurement, blood and urine sampling, standard 12-lead electrocardiogram, 24-h urine collection for microalbuminuria (MA), cardiac, carotid ultrasonography and two 24-h ABPMs at 1–4-week intervals.

The study protocol was approved by the Ethics Committee of one of the institutions involved.

Blood pressure measurements

Clinic BP was measured during two visits in the outpatient clinic using a mercury sphygmomanometer and taking the first and fifth Koroktoff sounds to identify systolic (SBP) and diastolic BP (DBP), respectively. Measurements started after the subjects had comfortably rested for 5 min in the sitting position.

Three measurements were taken at 1-min interval and the average was used to define clinic SBP and DBP. Heart rate was measured immediately thereafter by radial pulse analysis for 1 min.

Both ABPMs were carried out in the non-dominant arm using a Spacelabs 90207 device (Spacelabs Inc, Redmond, 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 (07.00–23.00 h) and at 20-min intervals during the night (23.00–07.00 h). In each patient, both ABPMs have been applied at the same time of the day (± 1 h). Patients were instructed to attend their usual activities and to keep the arm still at time of measurements; all patients were asked to go to bed no later than 23:00 h and to arise not before 07:00 h. All BP monitorings were performed on a working day (Monday to Friday). Recordings were analysed to obtain 24-h, daytime and night-time average SBP/DBP and heart rate. All subjects were classified in three groups according to the consistency of their average nocturnal BP values during the first and second ABPM session: (i) nocturnal normotension (NN) on both recordings (i.e. night-time SBP and DBP $< 120/70$ mmHg); (ii) NH on both recordings (i.e. night-time SBP and DBP $\geq 120/70$ mmHg); (iii) variable pattern (VP), i.e. NH in one and nocturnal normotension in the other ABPM.

Nocturnal non-dipping pattern was defined as a night-time reduction in SBP and DBP averages lower than 10% compared with daytime values.

Echocardiography

Technical details have been reported previously (24). In brief, M-mode, two-dimensional and Doppler echocardiographic examinations were performed with commercially available instruments. Left ventricular (LV) mass was estimated from end-diastolic LV internal diameter, inter-ventricular septum and posterior wall thickness according to Devereux's formula (25) and normalized to body surface area (BSA) or height$^{2.7}$ to obtain LV mass index.

Relative wall thickness was calculated as the ratio between posterior wall plus inter-ventricular septum thickness and LV internal diameter at diastole. LV filling was assessed by mitral flow with standard pulsed Doppler technique. The following parameters were considered: early diastolic peak flow velocity (E), late diastolic peak flow velocity (A) and their ratio (E/A).

Carotid ultrasonography

Images of extra-cranial carotid walls (common, bifurcation and internal carotid arteries) were obtained in several projections by high resolution, linear array 7.5–10.0-MHz probes.

Plaques were identified in the near and far wall of the extra-cranial carotid tree by the presence of focal wall thickening. Intima-media thickness was measured in the posterior wall of both common carotid arteries at 5, 10, 15, 20 and 25 mm caudally to the bifurcation (26). All five measurements were averaged to obtain the mean value of common carotid intima-media

thickness. Details about reproducibility of LV mass and intima-media thickness measurements in our laboratory have been previously reported (27).

Definition of organ damage

Organ damage was defined by the presence of MA, for urinary albumin excretion ranging from 30 to 300 mg/24 h (22), by ultrasonographic evidence of LV hypertrophy (LVH) and vascular alterations. In particular, LVH was defined as LV mass index equal to or higher than (i) 49 $g/m^{2.7}$ in men and 45 $g/m^{2.7}$ in women; (ii) 116 g/m^2 in men and 95 g/m^2 in women (28). The presence of one carotid atherosclerotic plaque, at least, or diffuse intima-media thickening was taken as evidence of vascular alteration; plaque was defined as a focal thickening greater than 1.3 mm in any segment of carotid arteries (29). Diffuse intima-media thickening was diagnosed when the average common carotid wall thickness exceeded 0.9 mm (22).

Statistical analysis

Statistical analysis was performed by the SAS system (version 6.12; SAS Institute Inc., Cary, NC, USA). Values were expressed as means ± SD or percentages.

Differences within groups were tested by analysis of variance (ANOVA). Analysis of categorical data was carried out by the χ^2 test or Fischer's exact test when appropriate. The strength of correlation between variables was tested by linear and multiple correlation analysis. The limit of statistical significance was set at $p < 0.05$. Sample size calculation indicated that the number of patients included in the study (477 NH, 119 VP, 62 NN) was sufficient to detect a 10 g/m^2 difference in LV mass index among the groups, with ± 20 g/m^2 standard deviation and 0.97 power at a 0.05 significance level.

Results

During the enrolment period, a total of 692 consecutive, never-treated, hypertensive subjects met the inclusion criteria; 658 of them (48% women) completed the study having valid ABPM (≥ 80% readings), cardiac and carotid ultrasonographic examinations. Mean age was 46 ± 12 years; 23% of study sample were current smokers (> 3 cigarette/day) and 12% were obese (body mass index ≥ 30 kg/m^2).

Approximately 5% of participants had an average 24-h BP < 125/80 mmHg during the first ABPM recording and 7% during the second, respectively, thus fulfilling the criteria for isolated clinic hypertension.

A total of 477 subjects had NH during the first ABPM period and exhibited the same pattern during the second period; 62 subjects had NN in both ABPM sessions. Overall, 119 subjects had a VP, as they changed their profile from one to the other ABPM session. Thus, 72.5% of subjects had reproducible NH, 18% VP and 9.5% reproducible NN. Figures for reproducible non-dipping, variable dipping and reproducible dipping status in the same population study were as follows: 24%, 24% and 52%.

As shown in the Table I, the different groups had similar age, gender distribution, current smoker prevalence, heart rate, total cholesterol, glucose, creatinine and uric acid levels.

Table I. Clinical characteristics of the study population according to the patterns of nocturnal blood pressure on two 24-h blood pressure monitorings within a 4-week interval: consistent nocturnal hypertension (NH), variable pattern (VP) and consistent nocturnal normotension (NN).

Variable	NN ($n = 62$)	VP ($n = 119$)	NH ($n = 477$)	p
Age (years)	46.9 ± 11.2	44.9 ± 13.7	46.5 ± 11.5	NS
Gender (% males)	53.2	61.3	63.5	NS
BSA (m^2)	1.80 ± 0.20[a]	1.86 ± 0.22	1.86 ± 0.21	<0.05
BMI (kg/m^2)	24.3 ± 3.6[a]	25.8 ± 4.1	25.4 ± 3.6	<0.01
Smoke (%)	17.7	26.0	23.1	NS
Clinic SBP (mmHg)	142 ± 14[a]	141 ± 14	147 ± 13	<0.001
Clinic DBP (mmHg)	92 ± 6[c]	93 ± 8[c]	97 ± 8	<0.001
Heart rate (b/min)	77 ± 11	75 ± 11	75 ± 10	NS
Total cholesterol (mg/dl)	213 ± 33	209 ± 39	216 ± 41	NS
HDL-cholesterol (mg/dl)	53 ± 18[a]	47 ± 16	48 ± 16	<0.05
Triglycerides (mg/dl)	105 ± 61[b]	119 ± 82	126 ± 76	<0.05
Glycemia (mg/dl)	93 ± 11	93 ± 11	93 ± 12	NS
Creatinine (mg/dl)	0.86 ± 0.1	0.87 ± 0.17	0.87 ± 0.17	NS
Uric acid (mg/dl)	4.8 ± 1.3	5.0 ± 1.4	4.9 ± 1.4	NS
UAE (mg/dl)	5.8 ± 7.5[b]	12.9 ± 34.5	13.0 ± 22.8	<0.05
MA (%)	3.4	5.8	8.7	NS

Data are shown as means ± SD or percentage; BSA, body surface area; BMI, body mass index; Smoke, current smokers (> 3 cigarettes/day); SBP, systolic blood pressure; DBP, diastolic blood pressure; HDL, high-density lipoprotein; MA, microalbuminuria; UAE, urinary albumin excretion. p-value: [a]NN vs VP and NH; [b]NN vs NH; [c]NN and VP vs NH.

Clinic SBP and DBP, body mass index, triglyceride and urinary albumin excretion values were significantly higher in the NH group as compared with NN group, whereas the opposite trend was observed for high-density lipoprotein-cholesterol. Intermediate values were observed in most instances in the VP group.

Data of both ABPMs are reported in Table II. Average 24-h, daytime and, by definition, night-time as well as the percentage fall in night-time SBP/DBP showed a progressive decrease from the NH to NN group. Conversely, prevalence rates of dippers and of subjects with isolated clinic hypertension showed the opposite trend.

The results of ultrasonographic studies are shown in Table III. End-diastolic LV internal diameter, interventricular septum, posterior wall thickness, aortic root, left atrium diameter, absolute LV mass, LV mass indexed either to BSA or to height$^{2.7}$ were higher in NH compared with NN. Differences between NH and VP group were weaker and attained statistical significance for posterior wall thickness, left atrium diameter and LV mass indexed to BSA. Mitral E/A ratio, common carotid intima-media thickness and diameter were similar across the groups.

Analysis of echocardiographic data as categories, namely presence/absence of LVH, showed a higher prevalence of LVH in NH compared with NN (Figure 1). In contrast, the percentage of subjects with carotid atherosclerosis and MA was superimposable in the three groups.

Categorical variables, such as gender and values below the median of age, body mass index, clinic, ambulatory BP, total cholesterol, LDL cholesterol, glucose, creatinine, MA, LVM index and carotid intima-media thickness were associated with NN phenotype by a logistic regression analysis with stepwise selection. Among these variables, only 24-h DBP (OR = 4.435, 95% CI 1.27–9.99, $p = 0.0003$), LVM index (OR = 3.28, 95% CI 1.49–7.16, $p = 0.003$) and 24-h SBP (OR = 3.23, 95% CI 1.14–8.21, $p = 0.02$) were independently correlated with NN phenotype.

Discussion

The present study in a large sample of untreated, non-diabetic hypertensive subjects free of overt CV disease, shows that persistent NH, defined by fixed cut-off limits suggested by current guidelines, occurs in the majority of the sample (i.e. > 70%), whereas consistent nocturnal normotension represents a marginal BP phenotype occurring in less than 10% of subjects.

Our findings, in keeping with previous observations, show that non-dipping and NH patterns may be dissociated (30,31); in our series, indeed, less than 50% of subjects with NH exhibited a non-dipping status. On the other hand, the dipping pattern is frequently associated with elevated nocturnal BP levels, thus suggesting that NH and dipping/non-dipping pattern may have different pathophysiological mechanisms.

Table II. Ambulatory blood pressure parameters of the study population according to the patterns of nocturnal blood pressure on two 24-h blood pressure monitorings within a 4-week interval: consistent nocturnal hypertension (NH), variable pattern (VP) and consistent nocturnal normotension (NN).

Variable	NN ($n = 62$)	VP ($n = 119$)	NH ($n = 477$)	p
First ABPM				
24-h SBP (mmHg)	126 ± 7[a]	130 ± 7[c]	139 ± 11	<0.001
24-h DBP (mmHg)	78 ± 5[a]	82 ± 6[c]	90 ± 8	<0.001
Daytime SBP (mmHg)	133 ± 8[a]	136 ± 9[c]	144 ± 11	<0.001
Daytime DBP (mmHg)	85 ± 6[a]	88 ± 6[c]	94 ± 8	<0.001
Night-time SBP (mmHg)	109 ± 7[a]	116 ± 8[c]	128 ± 11	<0.001
Night-time DBP (mmHg)	64 ± 4[a]	69 ± 6[c]	79 ± 8	<0.001
Nocturnal SBP decrease (%)	18 ± 5[a]	15 ± 5[c]	11 ± 5	<0.001
Nocturnal DBP decrease (%)	24 ± 5[a]	20 ± 7[c]	15 ± 6	<0.001
Dippers (%)	95[a]	80[c]	56	<0.001
Isolated clinic hypertension (%)	24[a]	11	1	<0.001
Diurnal hypertension (%)	76[b]	85	97	<0.001
Second ABPM				
24-h SBP (mmHg)	125 ± 7[a]	129 ± 7[c]	138 ± 10	<0.001
24-h DBP (mmHg)	78 ± 5[a]	81 ± 6[c]	89 ± 8	<0.001
Daytime SBP (mmHg)	132 ± 9[a]	135 ± 9[c]	143 ± 11	<0.001
Daytime DBP (mmHg)	84 ± 6[a]	87 ± 7[c]	94 ± 8	<0.001
Night-time SBP (mmHg)	109 ± 6[a]	114 ± 7[c]	127 ± 10	<0.001
Night-time DBP (mmHg)	64 ± 4[a]	69 ± 6[c]	79 ± 8	<0.001
Nocturnal SBP decrease (%)	17 ± 4[b]	15 ± 5[c]	11 ± 5	<0.001
Nocturnal DBP decrease (%)	23 ± 6[b]	20 ± 6[c]	15 ± 6	<0.001
Dippers (%)	94[b]	81[c]	55	<0.001
Isolated clinic hypertension (%)	32[a]	15[c]	1	<0.001
Diurnal hypertension (%)	66[b]	82	96	<0.001

Data are shown as means ± SD or percentage. p-value: [a]NN vs VP and NH; [b]NN vs NH; [c]VP vs NH.

Table III. Ultrasonographic findings of the study population according to the patterns of nocturnal blood pressure on two 24-h blood pressure monitorings within a 4-week interval: consistent nocturnal hypertension (NH), variable pattern (VP) and consistent nocturnal normotension (NN).

	NN ($n=62$)	VP ($n=119$)	NH ($n=577$)	p
LVIDd (mm)	46.3 ± 4.0^a	48.2 ± 4.4	48.2 ± 4.1	<0.01
LVIDs (mm)	27.0 ± 3.9^a	29.5 ± 4.6	28.9 ± 4.0	<0.001
IVSTd (mm)	9.3 ± 0.9^a	9.8 ± 1.2	10.0 ± 1.1	<0.001
PWTd (mm)	8.6 ± 0.9^a	8.9 ± 0.9^c	9.2 ± 0.9	<0.01
LV RWT	0.39 ± 0.05^d	0.39 ± 0.04	0.40 ± 0.05	<0.05
AR (mm)	31.4 ± 3.2^b	32.3 ± 3.6^b	33.1 ± 3.7	<0.05
LA (mm)	34.1 ± 4.4^d	34.9 ± 4.5	35.8 ± 4.5	<0.01
LVM (g)	160.9 ± 33.3^a	184.5 ± 42.5	191.4 ± 46.1	<0.001
LVM/BSA (g/m^2)	89.3 ± 16.7^a	98.5 ± 17.8^c	102.5 ± 19.7	NS
LVM/h ($g/m^{2.7}$)	38.8 ± 8.1^a	43.5 ± 9.2	44.8 ± 9.4	<0.01
E/A ratio	1.25 ± 0.38	1.25 ± 0.42	1.19 ± 0.37	NS
CC IMT (μm)	625 ± 120	620 ± 120	669 ± 140	NS
CC diameter (mm)	5.65 ± 0.66^d	5.85 ± 0.81	5.94 ± 0.69	0.01
Carotid Plaques (%)	21.1	18.2	22.0	NS

Data are shown as means ± SD or percentage; LVIDd, left ventricular internal diameter, diastole; LVIDs, left ventricular internal diameter, systole; IVSTd, interventricular septum thickness, diastole; PWTd, posterior wall thickness, diastole; RWT, relative wall thickness; LVM, left ventricular mass; LA, left atrium; AR, aortic root; E, early diastolic mitral flow; A, late diastolic mitral flow. LVH, left ventricular hypertrophy; LVM, left ventricular mass. LVMI, left ventricular mass index; CC, common carotid; IMT, intima-media thickness. p-value: [a]NN vs VP and NH; [b]NN and VP vs NH; [c]VP vs NH; [d]NN vs NH.

More pronounced degrees of subclinical cardiac damage were found in patients with NH as compared with their counterparts with normal nocturnal (NN) BP, despite the fact that in the former group dippers were more prevalent than non-dippers.

The study provides new evidence that a nocturnal BP drop large enough to normalize night-time BP is a rare finding in essential hypertension. This observation is strengthen by the fact that our series, according to a predefined protocol, did not include clinical conditions such as long-standing, severe or secondary hypertension, sleep apnea syndrome, type 1 and 2 diabetes, autonomic dysfunction, chronic renal disease and prevalent obesity, negatively affecting physiological circadian BP variations.

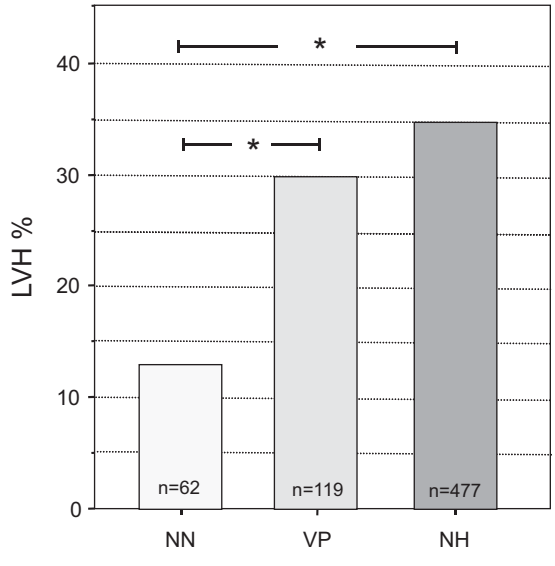

Figure 1. Prevalence of left ventricular hypertrophy (LVH, left ventricular mass index > 49/45 $g/h^{2.7}$ in men and women, respectively) in essential hypertensives divided in three groups according to nocturnal blood pressure cut-off value of 125/70 mmHg on two 24-h monitorings. NN, nocturnal normotension; VP, variable pattern; NH, nocturnal hypertension; $^*p < 0.01$.

To eliminate potential factors affecting nocturnal BP, we chose: (i) to include never-treated hypertensives; (ii) to recommend an effective 8-h bed-rest period at night in order to have sufficient BP recordings; (iii) to classify patients into three groups based on two ABPM sessions.

A likely consequence of the accurate definition of night-time BP profiles in our population is that NH/NN and dipping/non-dipping patterns represented true clinical traits. A limited reproducibility of circadian BP variations over time has been largely documented, and classification of dippers and non-dippers based on a single 24-h ABPM has been shown to be inaccurate (31–33). By our approach, we found that about 24% and 18% of subjects changed their nocturnal BP profile within a 4-week period as defined either by dipping/non-dipping categories or by fixed cut-off limits, respectively.

A notable aspect of our study is that the prevalence of persistent NH was about three-fold higher than the non-dipping pattern. Such a discrepancy between the two classifications may have practical implications for CV risk stratification and therapeutic strategies as dipping/non-dipping categories may underestimate the adverse role of increased nocturnal BP. A mounting body of evidence indicates that NH, defined by fixed cut-off partition values is more closely related to subclinical organ damage and CV prognosis than the non-dipping pattern (34–36). Dipping/non-dipping categories, indeed, are largely dependent on daytime BP values, which in turn are influenced by erratic factors including physical activity, mental stress, smoking and seasonal period (37).

A recent analysis of the International Database of Ambulatory Blood Pressure involving 8711 individuals from 10 populations showed that isolated NH (i.e. daytime BP $<$ 135/85 mmHg and night-time BP $\geq$ 120/70 mmHg) is associated with higher risks of total mortality (+ 29%, $p = 0.04$) and all CV events (+ 38%, $p = 0.003$) compared with nocturnal normotension (20). The independent prognostic value of nocturnal BP has been confirmed by an updated review of 24 prospective studies including 23,856 hypertensive patients and 9641 individuals from population-based cohorts, reporting that night-time SBP is a stronger predictor than daytime SBP (9).

Various mechanisms have been invoked to explain the enhanced CV risk associated with elevated night-time BP pressure, including impaired sympathetic modulation, decreased baroreflex sensitivity, altered circadian pattern of salt excretion (36). In addition, a more advanced target organ damage in patients with NH may contribute to blunt the vasodepressor influence of sleep.

A notable finding of our study is that in patients with NH, relative LV wall thickness, LM mass and LVH prevalence defined according to sex-specific criteria indexed either to BSA or to height to allometric power of 2.7 were significantly higher than in patients with consistent nocturnal normotension. It is worth noting that patients with NH during one of the ABPM sessions (i.e. VP group) had echocardiographic features similar to the NH group. A more pronounced LV involvement in NH was associated with a slight increase in urinary albumin excretion, although the prevalence of MA as well as of carotid atherosclerosis was not increased. These data do not exclude that extra-cardiac subclinical damage may be related to NH, but simply suggest that LV structural abnormalities, as assessed by echocardiography, are more sensitive markers of early organ damage in middle-aged grade 1 and 2 hypertensives.

Finally, the strength of the association between preclinical cardiac damage and nocturnal BP, independently of potential confounders, was supported by a logistic regression analysis showing that LV mass index below the median value was an independent correlate of nocturnal normotension.

There are some study limitations worth emphasizing. Our findings pertain to a cohort of uncomplicated Caucasian hypertensive subjects and the generalizability of the results to different clinical settings or other ethnic groups could not be determined. Our study did not assess physical activity and quality of sleep and the potential association of these covariates with the different patterns of nocturnal BP. The cross-sectional design of the study does not allow clarification of whether NH represents a risk factor or a risk marker of organ damage.

In conclusion, NH is a more common BP phenotype than the non-dipping pattern in early phases of uncomplicated essential hypertension. In a clinical perspective, the strong association between this phenotype and preclinical cardiac organ damage, independently of the dipping/non-dipping status, suggests that therapeutic options aimed to restore a blunted nocturnal BP fall may be insufficient to protect hypertensive subjects against the harmful effects of persistently elevated night-time BP values.

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