Original Article

Prevalence of isolated nocturnal hypertension according to 2018 European Society of Cardiology and European Society of Hypertension office blood pressure categories

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Objectives: To estimate the prevalence of isolated nocturnal hypertension (INH) and its relationships with office blood pressure (BP) categories defined by 2018 ESC/ESH guidelines.

Methods: We conducted a prospective cohort study in consecutive patients referred to perform an ambulatory blood pressure monitoring (ABPM) for diagnosis or therapeutic purposes. Office BP measurements and ABPM was performed in the same visit. The cohort was divided according to office BP in optimal, normal, high-normal and hypertension. The prevalence and adjusted risk for combined daytime and nocturnal hypertension and INH were estimated for each category.

Results: We evaluated 1344 individuals, 59.3% women (51 ± 14 years old) and 40.7% men (52 ± 15 years old). 61.5% of the individuals had nocturnal hypertension, 12.9% INH and 48.7% combined daytime and nocturnal hypertension. Prevalence of combined daytime and nocturnal hypertension increased through office BP categories ($P < 0.001$). Conversely, prevalence of INH was lower in individuals with hypertension than in normotensives (7.4 vs. 17.2%, $P < 0.001$) and similar between nonhypertensive office BP categories, 16.6, 15 and 19.4% for optimal, normal and high-normal BP, respectively ($P < 0.399$). In individuals with office BP values less than 140/90 mmHg, the prevalence phenotypes of masked hypertension were 8.6, 17.2 and 30.2% for daytime, INH and combined daytime and nocturnal hypertension, respectively. Adjusted risk for combined daytime and nocturnal hypertension increased significantly through office BP categories; conversely, the risk for INH was similar in all nonhypertensive office BP categories.

Conclusion: Nocturnal hypertension was the more prevalent phenotype of masked hypertension and more than one-third of the individuals with nocturnal hypertension had INH. The risk for INH was not related to nonhypertensive office BP categories.

Keywords: ambulatory blood pressure monitoring, isolated nocturnal hypertension, office blood pressure

Abbreviations: ABPM, ambulatory blood pressure monitoring; BP, blood pressure; CVD, cardiovascular disease; HOMA-IR, homeostasis model assessment of insulin resistance; INH, isolated nocturnal hypertension

INTRODUCTION

Ambulatory blood pressure monitoring (ABPM) complements office blood pressure (BP) because of its ability to quantify out-of-office BP and to evaluate BP values during night rest. Several distinct BP phenotypes can be determined as white coat and masked hypertension. In addition, the presence of nocturnal hypertension can be diagnosed. In the general population, nocturnal hypertension is a prevalent condition and implies an increased risk for cardiovascular disease (CVD) events and mortality [1–3]. Furthermore, in a large meta-analysis including 25 856 hypertensive patients and 9641 individuals randomly recruited from population-based cohorts night-time BP turned out to be a stronger predictor of outcomes than daytime BP, day–night BP ratio and nondipping pattern [4].

Li *et al*. coined the term isolated nocturnal hypertension (INH) for the first time in 2007 to describe a specific subtype of nocturnal hypertension characterized by elevated night-time BP (SBP $\geq$120 mmHg and/or DBP $\geq$70 mmHg) in the presence of normal daytime BP (SBP $<$135 mmHg and DBP $<$85 mmHg) [5]. Several published studies have shown that individuals with INH may have more arterial stiffness,

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cardiac damage and an increased risk of CVD events and mortality [6–9].

Most individuals with INH have normal office BP, so, it frequently is a 'masked' condition [10]. The confluence of increased organ damage, CVD events and mortality risk, and a failure to be diagnosed by conventional clinic BP measurement, makes INH a clinically important phenotype. Furthermore, a recently published study performed in children and young adults showed that 8% of the sample had masked INH, suggesting that the condition could be an early manifestation of hypertensive disease [11]. In this context, knowledge of the relationships among INH and data obtained at the clinical evaluation could be important in order to decide whether the search for nocturnal hypertension is necessary or not. However, this issue has not been extensively studied. In consequence, the aim of the present study was to estimate the prevalence of INH and its relationships with the office BP categories defined by 2018 European Society of Cardiology and European Society of Hypertension (ESC/ESH) guidelines [12].

MATERIAL AND METHODS

The sample included consecutively evaluated patients, between November 2013 and February 2019, at the Cardiometabolic Diseases Unit of Hospital San Martín (La Plata, Argentina). The patients were referred from clinics, cardiologists and general practice in order to perform an ABPM for diagnosis or therapeutic purposes. Written informed consent was obtained. Women with suspected hypertensive disorders of pregnancy were excluded. Only data from the first evaluation was analyzed.

The prospectively designed protocol for BP evaluation was as follows. Step 1: a specially trained nurse, at the end of a ~15 min interview, performed three BP measurements employing a validated oscillometric automatic BP device (OMRON HEM 705 CP; Omron, Kyoto, Japan) and cuff and bladder dimensions according to the arm circumference [12]. The measurements were made with the patient in a sitting position, with his back supported, without crossing the legs, with both feet on the floor, with the arm uncovered, supported and at heart level, and without speaking. Office BP was defined as an average of these three determinations; office hypertension was defined as BP at least 140/90 mmHg. Step 2: immediately after, an ABPM was initiated with a validated monitor (Spacelabs 90207; Spacelabs, Snowqualmie, Washington, USA). Measurements were scheduled every 15 min during the day and every 20 min at night. Only ABPMs with at least 70% successful measurements and at least one record per hour were considered valid. Night-time and daytime periods were defined taking into account the patient's schedule. INH was defined as a night-time SBP at least 120 mmHg and/or DBP at least 70 mmHg and a daytime BP less than 135/85 mmHg; isolated daytime hypertension was defined as a daytime SBP at least 135 mmHg and/or DBP at least 85 mmHg and a night-time BP less than 120/70 mmHg; combined daytime and nocturnal hypertension was defined as a night-time SBP at least 120 mmHg and/or DBP at least 70 mmHg and a daytime SBP at least 135 mmHg and/or DBP at least 85 mmHg; ABPM normotension was defined as a night-time BP less than 120/70 mmHg and a daytime BP less than 135/85 mmHg [5].

An epidemiological chart including self-reported antecedents of CVD, smoking, dyslipidemia, diabetes and antihypertensive drug use was performed. Weight was determined with individuals wearing light clothes and no shoes. Height was also measured without shoes, using a metallic metric tape. BMI was calculated using the formula weight (kg)/height^2 (m). Waist circumference was measured with a relaxed abdomen using a metallic metric tape on a horizontal plane above the iliac crest; neck circumference was measured in the middle of the neck, between the mid-cervical spine and the superior line of the cricothyroid membrane in a standing position. In order to evaluate the quality of habitual nocturnal resting, usual sleep duration, frequent arousals, loud snoring and unintentional daytime sleep were investigated.

The sample was divided according to 2018 ESC/ESH guidelines for the management of arterial hypertension in the following four office BP categories [12]: optimal, normal, high-normal and hypertension. The prevalence of isolated daytime, INH and combined daytime and nocturnal hypertension was estimated for each category of office BP in the whole sample, and separately in individuals with and without antihypertensive drugs.

The clinical characteristics of the ABPM phenotypes (normotension, isolated daytime hypertension, INH and combined daytime and nocturnal hypertension) were compared in individuals with office BP less than 140/90 mmHg, separately in untreated (masked hypertension) and treated individuals (masked uncontrolled hypertension).

Continuous variables were expressed as mean and standard deviation (SD); comparison between groups were made using one-way ANOVA with post hoc Bonferroni test. Categorical variables were expressed as percentage and were compared with χ^2 or Fisher's exact test.

The adjusted relative risks (compared with optimal office BP) for both, combined daytime and nocturnal hypertension and INH were estimated for each office BP category using binary logistic regression. The model-building process was made in two blocks. In the first block, the office BP categories were included; in the second block, covariates (age, sex, BMI, waist and neck circumferences, and antihypertensive drugs) were included using a conditional forward stepwise method (probability for stepwise, entry: 0.05, removal: 0.10). The adjusted relative risks were expressed as odd ratio (OR) with a confidence interval of 95% (95% CI).

Data were analyzed using SPSS and P values less than 0.05 (two-tailed) were considered significant.

RESULTS

One thousand, three hundred and seventy-two consecutive patients were evaluated; 28 were excluded because their ABPM did not meet prespecified quality criteria. The remaining 1344 individuals, 797 (59.3%) women, 51 ± 14 years old and 547 (40.7%) men, 52 ± 15 years old, were included in the present analysis. Mean office BP was 137 ± 18/ 82 ± 12 mmHg, mean BMI was 30.2 ± 5.8 kg/m^2; 14.1% were current smokers and 9.5, 8.1 and 3.2% had antecedents of diabetes, dyslipidemia and CVD, respectively.

TABLE 1. Characteristics of the individuals according to office blood pressure categories

	Office BP categories				
	Optimal ($n = 205$)	Normal ($n = 233$)	High normal ($n = 310$)	Hypertension ($n = 596$)	*P*
Age (years)	47 ± 16	49 ± 15	52 ± 16	54 ± 14	
Women (%)	77.1	66.7	54.2	54.5	<0.001
Antihypertensive drugs (%)	38.0	39.9	44.8	54.7	<0.001
Diabetes (%)	10.2	5.6	8.7	11.2	0.085
Dyslipidemia (%)	7.8	9.0	10.3	7.7	0.576
Previous CVD (%)	2.4	0.4	2.6	4.9	0.008
Current smoking (%)	14.8	18.0	11.6	13.6	0.192
BMI (kg/m^{2+})	29.1 ± 6.3	29.4 ± 5.8	30.4 ± 5.5	30.9 ± 5.7	<0.001
Waist circumference (cm)	97 ± 16	99 ± 14	102 ± 13	103 ± 15	<0.001
Neck circumference (cm)	38 ± 6	39 ± 5	39 ± 4	40 ± 7	<0.001
Systolic office BP (mmHg)	111 ± 7	124 ± 4	134 ± 4	153 ± 14	<0.001
Diastolic office BP (mmHg)	68 ± 7	75 ± 6	79 ± 8	90 ± 11	<0.001
Systolic diurnal ABPM (mmHg)	122 ± 12	129 ± 10	132 ± 11	142 ± 14	<0.001
Diastolic diurnal ABPM (mmHg)	76 ± 10	80 ± 8	82 ± 9	88 ± 12	<0.001
Systolic nocturnal ABPM (mmHg)	112 ± 14	116 ± 13	119 ± 12	128 ± 16	<0.001
Diastolic nocturnal ABPM (mmHg)	64 ± 9	67 ± 9	69 ± 10	75 ± 12	<0.001

Continuous variables expressed as mean ± standard deviation and proportions as percentage (%). ABPM, ambulatory blood pressure monitoring; BP, blood pressure.

In the overall study cohort, the prevalence of office BP categories were optimal 15.3%, normal 17.3%, high-normal 23.1% and hypertension 44.3%. Table 1 shows the characteristics of the individuals according to office BP categories. Obesity indicators and daytime and nocturnal ambulatory BP values increased through office BP categories.

According to the ABPM results, 827 (61.5%) of the individuals had nocturnal hypertension, 12.9% had INH and 48.7% had combined daytime and nocturnal hypertension. The prevalence of combined daytime and nocturnal hypertension increased thought office BP categories: 12.2, 33, 40 and 71.8% for optimal, normal, high-normal and hypertension respectively ($P < 0.001$). On the other hand, the prevalence of INH was lower in individuals with office hypertension than in normotensive ones (7.4 vs. 17.2%, $P < 0.001$), and similar between nonhypertensive office BP categories, 16.6, 15 and 19.4% for optimal, normal and high-normal BP, respectively ($P < 0.399$).

There were no statistically significant differences in the prevalence of diabetes ($P = 0.372$), current smoking ($P = 0.280$), and dyslipidemia ($P = 0.120$) between individuals with vs. without nocturnal hypertension. Individuals with nocturnal hypertension had more antecedents of previous CVD, 4.2 vs. 1.5%, $P = 0.007$. Although nocturnal hypertension was associated with higher values of neck circumference (40 ± 7 vs. 39 ± 4 cm, $P = 0.002$), other obesity indexes as BMI and waist circumference were similar ($P = 0.138$ and $P = 0.293$, respectively). Remarkably, no differences were found among individuals with vs. without nocturnal hypertension in the quality of habitual nocturnal resting: loud snoring (61.8 vs. 60.2%, $P = 0.550$), frequent arousals (5.7 vs. 6.0%, $P = 0.811$) or unintentional daytime sleep (4.2 vs. 4.6%, $P = 0.721$).

Six hundred and thirty-three individuals (47.3%) were on antihypertensive treatment when the ABPM was performed. The relationships of combined daytime and nocturnal hypertension and INH with office BP categories were similar in individuals with or without antihypertensive drug treatment (Fig. 1).

In individuals with office BP less than 140/90 mmHg ($n = 748$), the prevalence of different phenotypes of hypertension (masked hypertension) was 8.6, 17.2 and 30.2% for isolated daytime hypertension, INH, and combined daytime and nocturnal hypertension, respectively. The prevalence of INH was similar for treated vs. untreated patients (16 vs. 19%, $P = 0.277$). Remarkably, 129/173 (74.9%) of INH had normal office BP (masked INH). Comparing INH individuals with office hypertension, individuals with masked INH (office BP <140/90 mmHg) were younger (52 ± 16 vs. 59 ± 12 years old, $P = 0.006$) and less obese (BMI 30.5 ± 5.6 vs. 32.7 ± 6.8 kg/m^2, $P = 0.041$; waist circumference 102 ± 13 vs. 107 ± 14 cm, $P = 0.026$). There was no difference in sex ($P = 0.705$), current smoking ($P = 0.211$) and self-reported antecedents of diabetes ($P = 0.962$), dyslipidemia ($P = 0.140$) and CVD ($P = 0.846$).

Characteristics of individuals with masked hypertension are shown in Tables 2 and 3. Table 2 shows the clinical characteristics of untreated individuals and Table 3 shows the clinical characteristics of treated and controlled individuals according to ABPM phenotypes. Remarkably, patients without antihypertensive treatment with masked combined daytime and nocturnal hypertension, compared with normotensive individuals, had higher values of office BP. Conversely, patients with isolated nocturnal hypertension had similar levels of office BP but higher values of neck circumference.

The logistic regression analysis showed that adjusted risk combined daytime and nocturnal hypertension increased significantly through office BP categories; conversely, the risk of INH was similar in all nonhypertensive office BP categories and lower in patients with office hypertension (Table 4). In the multivariate models with INH as dependent variable, only age, waist circumference and neck circumference were statistically significant covariates. Remarkably, the logistic regression models including office blood pressure categories and covariates predict better the risk for combined daytime and nocturnal hypertension than the risk for INH (−2 log likelihood = 1570.65, Cox and Snell $r^2 = 0.146$, Nagelkerke $r^2 = 0.198$ vs. −2 log

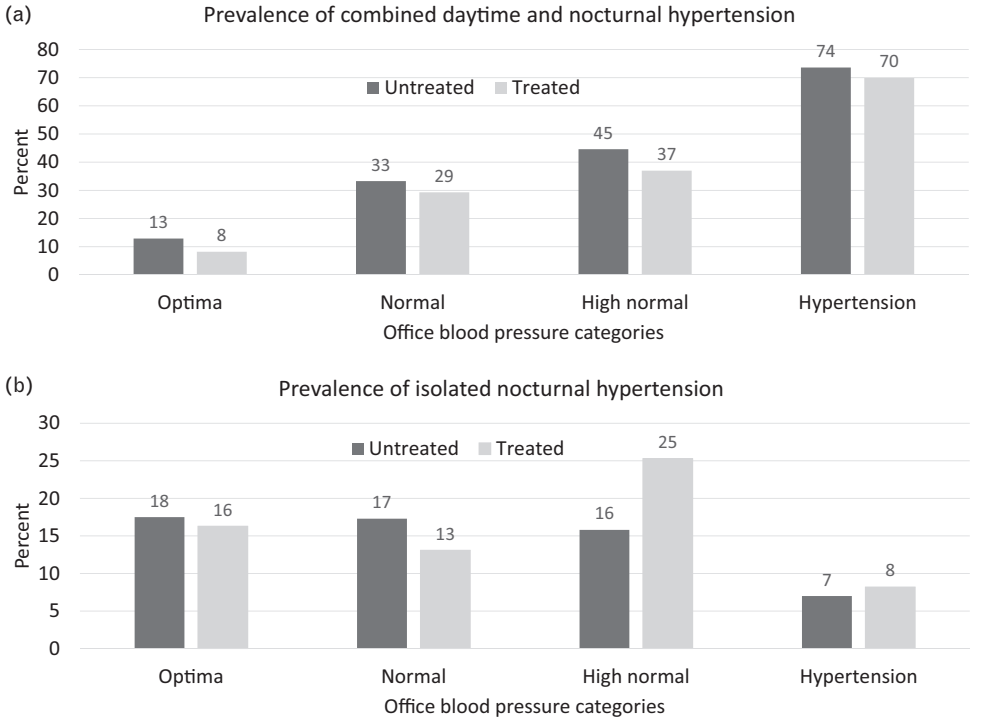

FIGURE 1 Prevalence of combined daytime and nocturnal (a) and isolated nocturnal (b) hypertension according 2018 European Society of Cardiology and European Society of Hypertension office blood pressure categories in individuals with and without antihypertensive drug treatment.

likelihood = 983.23, Cox and Snell $r^2 = 0.034$, Nagelkerke $r^2 = 0.064$)

DISCUSSION

In a recently published population-based study from Australia, Head *et al.* [13] showed that masked hypertension was a much more frequent cause of office misdiagnosis than white-coat hypertension (21 vs. 3%). On the basis of these results, the authors highlight the importance of out-of-office BP assessments in order to effectively diagnose and treat hypertension. Our study shows that nocturnal hypertension was the most prevalent phenotype of masked hypertension and more than one-third of the individuals with nocturnal hypertension had normal ABPM during daytime activities, namely INH. Remarkably, the risk for this subtype of nocturnal hypertension was not related with nonhypertensive office BP categories.

The prevalence of INH in our study was 12.9%, a little higher to the prevalence reported in prior studies in population samples (6–10.9%) [10]. This difference could be because of a selection bias as our study was performed in patients referred in order to perform an ABPM for diagnostic or therapeutic purposes. In addition, previously published studies showed regional variations in the INH prevalence. In a multi-ethnic study, the prevalence was

TABLE 2. Clinical characteristics of the normotensive untreated individuals at office according to ambulatory blood pressure monitoring phenotypes

	Ambulatory blood pressure monitoring phenotypes						
	Normal ($n = 181$)	Isolated daytime ($n = 45$)	Isolated nocturnal ($n = 70$)	Daytime and nocturnal ($n = 142$)	*P*	P^a	P^b
Age (years)	47 ± 16	42 ± 12	47 ± 18	46 ± 15	0.307	–	–
Women (%)	64.6	42.2	57.1	58.5	0.052	0.271	0.255
Diabetes (%)	7.2	2.2	8.4	4.2	0.358	0.709	0.262
Current smoking (%)	13.8	13.3	20.0	20.4	0.338	0.225	0.114
Frequent arousals (%)	7.2	4.4	5.7	6.3	0.913	0.786	0.765
Unintentional daytime sleep (%)	5.0	6.7	8.6	4.9	0.686	0.281	0.986
Loud snoring	55.2	46.7	52.9	54.9	0.760	0.733	0.954
BMI (kg/m^2)	29.8 ± 5.8	27.7 ± 4.2	29.9 ± 5.1	28.6 ± 5.6	0.045	1.00	0.359
Waist circumference (cm)	98 ± 16	95 ± 12	100 ± 14	98 ± 15	0.230	-	-
Neck circumference (cm)	38 ± 3	38 ± 3	40 ± 9	38 ± 4	0.005	0.003	1.00
Systolic office BP (mmHg)	121 ± 11	129 ± 7	123 ± 12	127 ± 9	<0.001	0.917	<0.001
Diastolic office BP (mmHg)	73 ± 8	78 ± 7	74 ± 10	78 ± 7	<0.001	1.00	<0.001

Continuous variables expressed as mean ± standard deviation and proportions as percentage (%). BMI, body mass index; BP, blood pressure.
[a]Normal vs. isolated nocturnal hypertension.
[b]Normal vs. combined daytime and nocturnal hypertension.

TABLE 3. Clinical characteristics of the treated and controlled (Office BP <140/90 mmHg) individuals according to ambulatory blood pressure monitoring phenotypes

	Ambulatory blood pressure monitoring phenotypes						
	Normal ($n = 148$)	Isolated daytime ($n = 19$)	Isolated nocturnal ($n = 59$)	Daytime and nocturnal ($n = 84$)	*P*	P^a	P^b
Age (years)	54 ± 13	51 ± 17	56 ± 13	54 ± 17	0.589	–	–
Women (%)	75.7	68.4	54.2	66.7	0.026	0.002	0.140
Diabetes (%)	13.5	5.3	15.3	6.0	0.192	0.745	0.082
Current smoking (%)	12.8	26.3	6.8	7.1	0.059	0.326	0.179
Frequent arousals (%)	4.7	5.3	8.5	4.8	0.737	0.329	1.0
Unintentional daytime sleep (%)	4.1	0	3.4	2.4	0.764	1.0	0.714
Loud snoring	65.5	68.4	79.7	61.9	0.143	0.046	0.579
BMI (kg/m^2)	31.3 ± 6.5	28.2 ± 6.0	31.3 ± 6.2	29.0 ± 5.2	0.011	1.00	0.039
Waist circumference (cm)	103 ± 15	96 ± 13	104 ± 12	100 ± 12	0.097	–	–
Neck circumference (cm)	39 ± 6	37 ± 3	40 ± 4	39 ± 5	0.208	–	–
Systolic office BP (mmHg)	122 ± 11	127 ± 9	127 ± 11	130 ± 7	<0.001	0.005	<0.001
Diastolic office BP (mmHg)	72 ± 7	75 ± 11	76 ± 9	78 ± 9	<0.001	0.083	<0.001

Continuous variables expressed as mean ± standard deviation and proportions as percentage (%). BP, blood pressure.
[a]Normal vs. isolated nocturnal hypertension.
[b]Normal vs. combined daytime and nocturnal hypertension.

higher in Chinese (10.9%), Japanese (10.2%), and South Africans (10.5%) than in Western (6.0%) and Eastern Europeans (7.9%) [10]. Thus, a higher prevalence could be because of environmental and/or ethnic factors.

In our study, in treated individuals with normal office BP (apparently controlled hypertension), the prevalence of INH was 19%, very close to the value communicated by Gorostidi *et al.* [14] using data from the Spanish Society of Hypertension ABPM Registry (19.3%) [14]. More recently, Banegas *et al.* [15] found, in patients with masked uncontrolled hypertension from the same database, a prevalence of INH of 24.3%. Thus, the prevalence values of our study in both treated and untreated individuals, seems reasonably comparable with those of previously published studies.

Although the reproducibility of nocturnal hypertension has been questioned [16], the relationships between nocturnal high BP values and CVD events and mortality are now widely proved [1–4]. Moreover, increasing evidence supports in a specific manner the importance of INH for the development of CVD. Li *et al.* [6] showed for a Chinese population that INH was associated to increased arterial stiffness. In the Jackson Heart Study, INH was associated to increased left ventricular mass compared with normotension in a population-based cohort of African Americans [8]. Similar results were communicated by Cuspidi *et al.* [7] in Italian participants of the Pressioni Arteriose Monitorate E Loro Associazioni (PAMELA) study. In 165 hypertensive patients with well controlled self-measured BP, INH was associated to increased carotid intima–media thickness and relative wall thickness [17]. In a recently published study, INH was observed in 13% of children with chronic kidney disease and was associated to alterations in arterial morphology and function [18]. We have shown that, in women with high-risk pregnancies, INH predicts the subsequent development of preeclampsia [19,20].

The mechanisms of organ damage in patients with INH are still not fully understood but some authors postulated that this form of high BP might be a pathophysiologically distinct clinical entity [10]. In the same direction, our working group have shown that individuals with INH, compared with those with isolated daytime hypertension, had significantly higher levels of three insulin resistance markers: fasting plasma insulin, homeostasis model assessment of insulin resistance (HOMA-IR) and triglycerides/high-density lipoprotein cholesterol ratio [21]. Thus, insulin resistance could be a linchpin between nocturnal hypertension and CVD. In our study, the regression analysis showed that waist circumference was a significant covariate for INH, supporting this possibility.

Obstructive sleep apnea has been associated with nocturnal hypertension; the absence of polysomnographic data is a limitation of our study. Furthermore, although some

TABLE 4. Absolute risks and adjusted odds ratios for combined, daytime and nocturnal hypertension, and isolated nocturnal hypertension according to 2018 European Society of Cardiology and European Society of Hypertension office blood pressure categories

	Combined daytime and nocturnal hypertension			Isolated nocturnal hypertension		
		Adjusted relative risk[a]			Adjusted relative risk[b]	
Office BP	Absolute risk (%)	OR	95% CI	Absolute risk (%)	OR	95% CI
Optimal	12.2	1.00		16.6	1.00	
Normal	33.0	2.27	1.52–3.39	15.0	0.83	0.50–1.40
High normal	40.0	3.63	2.47–5.34	19.4	1.04	0.65–1.67
Hypertension	71.8	9.71	6.69–14.10	7.4	0.32	0.20–0.53

P values for covariates: significance of the change. BP, blood pressure.; CI, confidence interval; OR, odds ratio.
[a]Model summary: −2 log likelihood = 1570.65, Cox and Snell $r^2 = 0.146$, Nagelkerke $r^2 = 0.198$. Covariates included in the equation: BMI ($P < 0.001$) and neck circumference ($P = 0.009$). Covariates excluded: age ($P = 0.632$), sex ($P = 0.764$), waist circumference (0.100) and antihypertensive drugs ($P = 0.281$).
[b]Model summary: −2 log likelihood = 983.23, Cox and Snell $r^2 = 0.034$, Nagelkerke $r^2 = 0.064$. Covariates included in the equation: age ($P = 0.045$), waist circumference ($P = 0.039$) and neck circumference ($P = 0.07$). Covariates excluded: BMI ($P = 0.788$), sex ($P = 0.861$) and antihypertensive drugs ($P = 0.854$).

data related to the quality of sleep were recorded, no specific questionnaire was used. In a recently published study, undiagnosed sleep apnea was found in 72.9% patients (29.3% mild, 26.6% moderate, 17.0% severe) of 188 patients with nocturnal hypertension [22]. In our cohort, neck circumference, a risk factor for obstructive sleep apnea, was also higher in individuals with INH suggesting that it could partially explain higher nocturnal BP values. However, the symptoms of inappropriate nocturnal resting (loud snoring, frequent arousals and unintentional daytime sleep) do seem similar among individuals with vs. without INH. Thus, although obstructive sleep apnea could be a cause for nocturnal hypertension, other mechanisms may be involved.

The INH prognosis was investigated using the International Database on Ambulatory Blood Pressure in relation to Cardiovascular Outcomes (IDACO) in 8711 individuals from 10 populations. During a median follow-up of 10.7 years, 1284 participants died and 1109 experienced fatal and nonfatal CVD events. Patients with INH had higher rates of all-cause and cardiovascular mortality and CVD events [9].

Thus, INH arises as an emerging mechanism for the cardiovascular damage observed in individuals with BP below the traditional hypertensive threshold. In this sense, Lawes *et al.* estimated that one-half of the high BP attributable burden of disease occurred in individuals with SBP levels less than 140 mmHg [23]. Furthermore, in our study, INH was a frequent finding in treated and apparently controlled hypertensive patients. This finding could be related to the residual risk previously described in treated patients [24].

Interestingly, our study shows that the relationships among combined daytime and nocturnal and INH with office BP values were different. Although the risk for combined daytime and nocturnal hypertension increased with higher office BP values, this was not the same for INH. First, most of the individuals who had INH had office BP less than 140/90 mmHg. Furthermore, the prevalence of INH was not significantly different in individuals with optimal, normal and high-normal BP. Finally, in regression logistic models, office BP categories predicts the possibility of combined daytime and nocturnal hypertension but not of INH. This lack of relation between office BP categories and INH increases the difficulties in the task of identifying the patients at risk because performing ABPM routinely in individuals with normal office BP is not feasible in the clinical practice. Therefore, the phrase from a title of Li and Wang [10] 'Isolated nocturnal hypertension: a disease masked in the dark' continues to be appropriate.

There are several limitations in this study that must be recognized. Firstly, some bias inherent to the experimental design (consecutive patients) could occur and prevalence values should not be extrapolated to general population. Secondly, the results are based on one BP monitoring only and short-term reproducibility has been questioned [16]. However, in an analysis of hypertensive patients enrolled in a placebo-controlled clinical trial the reproducibility of nocturnal hypertension was much higher than nondipping pattern [25]. Finally, and more importantly, it is not known whether treating this condition would reduce the risk of CVD and mortality.

In conclusion, despite these limitations, our results show that nocturnal hypertension was the more prevalent phenotype of masked hypertension and more than one-third of the individuals with nocturnal hypertension presented the subtype INH. The INH should be taken into consideration in individuals with organ damage and normal office BP values, irrespectively of the antihypertensive treatment status or office BP category.

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Conflicts of interest

There are no conflicts of interest.

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