ORIGINAL ARTICLE

Nocturnal Hypertension: Analysis According to its Severity

Hipertensión arterial nocturna: análisis según su gravedad

JOAQUÍN PEREA[1,2], DAMIÁN JESÚS MALANO[1], EVELYN ANABELLA FIORI[1], CAMILA MUSLERA[1], DANIEL MARTÍN[1], OSCAR GÓMEZ[1], DIEGO MARTÍN ARLUNA[1], BRIAN TOMÁS PEROTTI[1], MARLON ALFONSO RUIZ HOLGUÍN[1], ÁLVARO SOSA LIPRANDI[1,2, MTSAC]

ABSTRACT

Background: In the diagnosis and follow-up of arterial hypertension (HTN) most practice guidelines recommend ambulatory blood pressure monitoring (ABPM). In this regard, there is increasing evidence supporting the superiority of nocturnal hypertension (NHTN) as a predictor of cardiovascular events. Little is known about the relationship with cardiovascular events according to the severity of NHTN. Furthermore, it is unclear from what nighttime pressure value the risk begins to increase.
Objectives: The aim of this study was to determine whether the presence of NHTN and its severity levels are associated with adverse cardiovascular outcomes during follow-up.
Methods: An observational study was performed analyzing data collected from 24-hour ABPM studies obtained in a high complexity medical center in Buenos Aires. We examined patients' clinical characteristics, laboratory findings, imaging studies and their results during the follow-up period. Our study included ≥18 year-old persons who had been diagnosed with hypertension. We defined NHTN as those cases with blood pressure values ≥120/70 mmHg during the nighttime period.
Results: The final analysis included 981 patients. Among these, 53 % were men, mean age was 59.4 years and NHTN was present in 63.6 % of cases (n=624). Nocturnal HTN was classified into four severity strata for comparison, according to the nighttime systolic blood pressure value: 83-119 mmHg, 120-139 mmHg, 140-159 mmHg and 160-220 mmHg. Major adverse cardiovascular events were recorded in 8 (2.2 %), 17 (4.1 %), 8 (5.6 %) and 7 (11.3 %) subjects, respectively, and this difference between groups was statistically significant (p=0.007). Multivariate Cox regression analysis showed that the presence of NHTN was an independent predictor of adverse cardiovascular events (HR 3.60; 95% CI 1.12-11.5; p=0.033), even when considering the presence of daytime hypertension.
Conclusion: In this contemporary cohort, NHTN and its severity were independently associated with the incidence of adverse cardiovascular events.

Key words: Hypertension - Nocturnal hypertension - Coronary Heart Disease - Ambulatory Blood Pressure Monitoring

RESUMEN

Introducción: En el diagnóstico y seguimiento de la hipertensión arterial (HTA) la mayoría de las guías de práctica recomiendan el monitoreo ambulatorio de la presión arterial (MAPA). En este sentido, existe cada vez más evidencia que respalda la superioridad de la hipertensión arterial nocturna (HTAN) como predictor de eventos cardiovasculares. Se sabe poco sobre la relación con los eventos cardiovasculares según la gravedad de la HTAN. Además, no está claro a partir de qué valor de presión arterial nocturna comienza a aumentar el riesgo.
Objetivos: Conocer si la presencia de HTAN y sus niveles de gravedad se asocian con resultados cardiovasculares adversos durante el seguimiento.
Material y métodos: Estudio observacional. Realizamos un análisis de los datos obtenidos en un centro médico de alta complejidad de Buenos Aires, recopilados a partir de estudios de MAPA de 24 horas. Examinamos las características clínicas de los pacientes, los resultados de laboratorio, los estudios de imagen y sus resultados durante el período de seguimiento. Nuestro estudio incluyó personas de 18 años o más a las que se les había diagnosticado hipertensión. Definimos HTAN como aquellos casos con valores de presión arterial ≥ 120/70 mmHg durante el periodo nocturno.
Resultados: Fueron incluidos 981 pacientes en el análisis final. De ellos, el 53 % eran hombres; la edad media era de 59,4 años. Presentaban HTAN 63,6 % (n=624). Clasificamos la HTAN en cuatro estratos de gravedad para comparar, según el valor de presión arterial sistólica nocturna: 83-119 mmHg, 120-139 mmHg, 140-159 mmHg y 160-220 mmHg. Se registraron eventos adversos cardiovasculares mayores en 8 (2,2 %), 17 (4,1 %), 8 (5,6 %) y 7 (11,3 %) sujetos, respectivamente, y esta diferencia entre grupos fue

Rev Argent Cardiol 2024;92:263-270. http://dx.doi.org/10.7775/rac.v92.i4.20798

SEE RELATED ARTICLE: Rev Argent Cardiol 2024:92:261-262. http://dx.doi.org/10.7775/rac.v92.i4.20793

Received: 06/03/2024 – *Accepted:* 07/10/2024

Correspondence: Joaquín Perea. E-mail: joacoperea33@gmail.com. Research Department Sanatorio Güemes. Francisco Acuña de Figueroa 1228, 7th Floor, CP 1180AAX, City of Buenos Aires, Argentina

[1] Cardiology Service, Sanatorio Güemes.
[2] Research Department, Sanatorio Güemes.

estadísticamente significativa (p=0,007). El análisis multivariado de regresión de Cox demostró que la presencia de HTAN fue un predictor independiente de eventos cardiovasculares adversos (HR 3,60; IC 95% 1,12-11,5; p=0,033), incluso al considerar la presencia de hipertensión arterial diurna.
Conclusión: En esta cohorte contemporánea, la HTAN y su gravedad se asociaron independientemente con la incidencia de eventos cardiovasculares adversos.

Palabras clave: Hipertensión arterial- Hipertensión arterial nocturna - Enfermedad cardiovascular - Monitoreo ambulatorio de presión arterial

INTRODUCTION

The global prevalence of atherosclerotic cardiovascular disease continues to rise due to the increase of risk factors such as obesity, unhealthy lifestyles and population aging. (1,2) Hypertension (HTN) is recognized as one of the most significant risk factors, and has a high worldwide prevalence; therefore, it is crucial to make a correct diagnosis and treatment. (3)

Most international guidelines recommend ambulatory blood pressure monitoring (ABPM), which has become essential for the management of patients with HTN, not only for initial diagnosis but also for follow-up and subsequent control. (4-7) Most studies have shown that 24-hour average blood pressure is a better predictor of cardiovascular events than office blood pressure measurement. (8) In this context we have increasing evidence supporting the superiority of nocturnal hypertension (NHTN) as a predictor of cardiovascular events relative to daytime hypertension, so that ABPM has become essential not only for detection but also for determining its severity. (9,10) There is scarce information about the value of the degree of blood pressure elevation during the nighttime period and its relationship with cardiovascular events and, moreover, from what value of nighttime blood pressure the risk of cardiovascular events begins to increase.

The aim of this study was to find out whether the presence of NHTN and its severity levels are associated with the incidence of cardiovascular adverse events during follow-up.

METHODS

Study design

A retrospective cohort study was conducted including patients who underwent 24-hour blood pressure monitoring for diagnostic confirmation of HTN, or for prognostic purposes, in hypertensive subjects, in a hospital of the Autonomous City of Buenos Aires, Argentina, from March 2017 to December 2022. The composite of adverse cardiovascular events, the so-called major adverse cardiovascular events (MACE) which include cardiovascular death, nonfatal infarction and nonfatal stroke; and hospitalization or visit to the emergency department for heart failure (defined by Framingham criteria), was considered as primary endpoint. Each component of the primary endpoint, in addition to hospitalization for hypertensive urgency/emergency, were considered secondary endpoints.

Study population and definitions

We created our own database, including patients over 18 years of age who underwent pressure monitoring in the Cardiology department.

The variables included in the registry were: a) personal data, gender, age, weight in kg, body mass index (BMI) expressed in kg/m^2 (DuBois formula), medical history and classical cardiovascular risk factors; b) from the pressure monitoring data: study date, percentage of successful readings, 24-h averages, daytime and nighttime averages, pulse pressure, nocturnal pattern of blood pressure behavior (dipper, non-dipper, inverted dipper, or hyper dipper); c) laboratory data: creatinine value prior to the study, creatinine clearance value according to the Cockroft-Gault formula, and values at follow-up; d) echocardiographic data: atrial size, septal thickness, posterior wall thickness, left ventricular ejection fraction (LVEF) by Simpson's method; e) antihypertensive treatment with specification of drugs used, use of statins and aspirin.

Patients with technically unsatisfactory studies, duplicate pressure monitoring reports (the first record was included) and those in whom follow-up data could not be obtained were excluded. Follow-up was performed through the institution's electronic medical record.

Nocturnal HTN was defined according to the criteria of the American Heart Association (AHA) taking as reference a blood pressure value ≥120/70 mmHg during the passive/nighttime period, and a value ≥135/85 mmHg in the active/daytime period, both referred in the follow-up chart. (11) We classified NHTN into four severity strata according to nighttime systolic blood pressure: 83-119 mmHg (normal blood pressure), 120-139 mmHg, 140-159 mmHg and 160-220 mmHg.

Procedures

MEDITECH® pressure gauges (model ABPM 05) were used, with oscillometric method and ±3 mmHg accuracy/2 % of the measured value according to the manufacturer's technical specifications. They were programmed to take measurements every 15 minutes during the active period and every 30 minutes during the passive period, for 24-hour intervals. Data collection analysis and reporting software was provided by the manufacturer. Follow-up was performed by a group of 4 investigators by consulting the institutional electronic medical record; in cases where the data were incomplete or absent, contact and follow-up were made by telephone and closed-ended questions, for a maximum period of 48 months after the index pressure monitoring.

Statistical analysis

Statistical analyses were performed with R Studio, version 1.4.1106 (The R Foundation for Statistical Computing, Vienna, Austria). Continuous variables are expressed as mean and standard deviation (SD) or median and interquartile range (IQR), according to their distribution. Qualitative variables are expressed as absolute and relative frequencies. Qualitative variables were compared using the chi-square test or Fisher's exact test, while continuous variables with parametric and nonparametric distribu-

tion were compared using Student's t test and the Mann Whitney U test, respectively. Multiple imputation of the database was performed for the treatment of missing data, which was carried out through the random forest method since most of the variables imputed were categorical. (12) Bivariate and multivariate analyses were performed to identify factors associated with cardiovascular events. Cox regression models were used to search for predictors of events in the long-term follow-up. All variables that in the bivariate analysis presented a p value <0.20 or that were considered clinically important in relation to the response variable were included in the multivariate model. Nested models were compared and chosen according to Akaike's information criterion, ANOVA and concordance index. Kaplan Meier curves and the log-rank test were performed for variables associated with events at follow-up. The association between predictors and the incidence of events was expressed as Hazard Ratio with its 95% confidence interval (95% CI). All tests were two-tailed and statistical significance was established at $p<0.05$.

RESULTS

Baseline population characteristics

Out of a total of 1060 initial subjects, 79 cases were excluded from the analysis (60 did not meet the definition of HTN and 19 did not present follow-up). A total of 981 patients remained as the study population. Fifty-three percent were male, and mean age was 59.8±14.2 years. The baseline characteristics of the population stratified according to nighttime systolic blood pressure are shown in Table 1. NHTN was present in 63.6% of the subjects (n= 624). This group had higher BMI, greater prevalence of male gender, diabetes (DM), and as expected, higher daytime systolic and diastolic blood pressure. In the stratified analysis according to the severity of NHTN, we found a positive gradient with respect to cardiovascular risk factors, that is, the higher the degree of nighttime blood pressure, the higher the BMI and the greater the prevalence of DM, sedentary lifestyle and dyslipidemia. Those with higher nighttime blood pressure values had a more frequent history of atrial fibrillation, obstructive sleep apnea-hypopnea syndrome (OSAHS) and echocardiographic repercussion. Patients with NHTN had a lower use of antihypertensive drugs (76 % vs. 86 %, $p<0.001$). In this group, the most commonly used antihypertensive drugs were angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers.

Events by group

At a median follow-up of 40 (IQR 26-54) months, the main endpoint was present in 130 subjects corresponding to 13.2 % of the total sample, 105 (15.3 %) in the group with NHTN and 25 (8.3 %) in the group without NHTN ($p=0.003$). In the stratified analysis according to the degree of HTN we found differences between groups in the incidence of: a) the primary endpoint: from 7.6 % between 83-119 mmHg to 24.2 % between 160-220 mmHg ($p=0.001$); b) MACE: from 2.2 % between 83-119 mmHg to 11.3 % between 160-220 mmHg ($p=0.007$); c) hospitalization for heart failure: from 1.1 % between 83-119 mmHg to 8.1 % between 160-220 mmHg ($p=0.002$), and d) hospitalization for hypertensive crisis: from 2.5 % between 83-119 mmHg to 4.8 % between 160-220 mmHg, ($p=0.007$). Regarding cardiovascular death, although the proportion was higher in the NHTN group, there were no statistically significant differences: from 2.2 % between 83-119 mmHg to 8.1 % between 160-220 mmHg ($p=0.102$). The probability of event-free survival according to the presence of NHTN, and of the primary endpoint, MACE and hospitalization for heart failure according to the severity of NHTN is shown in Figure 1.

Multivariate analysis: independent predictors of cardiovascular events

We excluded from the multivariate analysis DM, BMI, OSAHS variables and HTN patterns because they presented a p value >0.20 in the bivariate analysis (Table 2). The remaining variables were evaluated in multivariate analysis with the Cox proportional hazards model. Two regression models were fitted and compared with each other. Model 1 included the NHTN strata, age, smoking, left ventricular hypertrophy, and daytime HTN; and model 2 the same variables except for daytime HTN. The latter model showed the best fit (Table 3), including the severity of NHTN variable as an independent predictor of cardiovascular events, with HR (95% CI) 1.30 (0.65 - 2.58), 2.25 (1.02 - 4.94) and 4.18 (1.60 -10.8) for 120-139, 140-159 and 160-220 mmHg strata, respectively. The NHTN behaved as an independent predictor of cardiovascular events (HR 3.60 95% CI 1.12-11.5 $p=0.033$). Age and presence of left ventricular hypertrophy in the echocardiogram also behaved as independent predictors, with HR (95% CI) 1.04 (1.01-1.06) and 2.35 (1.32-4.20), respectively. When adjusted for the presence of daytime HTN, the severity of NHTN remained as an independent predictor of events, so due to the principle of parsimony it was eliminated from the final model. All the adjusted models complied with the proportional hazards assumptions.

DISCUSSION

The main finding of our study is the high prevalence of NHTN and its association with cardiovascular outcomes at the long-term follow-up. We observed that this risk begins in the first severity stratum (120-139 mm Hg) and increases exponentially through each stratum, with the highest risk in the highest severity one (160-220 mm Hg). The severity of NHTN behaved as an independent predictor of adverse cardiovascular outcomes, even in the presence of the daytime HTN variable. Age and left ventricular hypertrophy variables in the echocardiogram were also factors associated with poor outcome.

Hypertension is the main modifiable risk factor,

Tabla 1. Baseline characteristics of the population stratified according to nocturnal systolic blood pressure

	83-119 mmHg	120-139 mmHg	140-159 mmHg	160-220 mmHg	p
n	357	419	143	62	
Male gender, n (%)	186 (52.1)	222 (53.0)	76 (53.1)	38 (61.3)	0.612
Age, mean (SD)	59.73 (13.37)	58.96 (14.65)	61.90 (14.79)	61.61 (14.42)	0.133
BMI, median (IQR)	28 (25-31)	29 (26-32.43)	30 (27-34)	33.16 (29.40-36.80)	<0.001
Diabetes, n (%)	36 (10.1)	68 (16.2)	38 (26.6)	24 (38.7)	<0.001
Dyslipidemia, n (%)	139 (38.9)	131 (31.3)	47 (32.9)	28 (45.2)	0.045
Sedentary lifestyle, n (%)	208 (58.3)	244 (58.2)	83 (58.0)	52 (83.9)	0.001
Smoking, n (%)	87 (24.4)	82 (19.6)	26 (18.2)	14 (22.6)	0.303
History of ACS, n (%)	23 (6.4)	25 (6.0)	9 (6.3)	6 (9.7)	0.743
History of stroke, n (%)	16 (4.5)	21 (5.0)	2 (1.4)	4 (6.5)	0.253
History of CHF, n (%)	5 (1.4)	6 (1.4)	1 (0.7)	2 (3.2)	0.579
History of AF, n (%)	4 (1.1)	16 (3.8)	4 (2.8)	7 (11.3)	<0.001
OSAHS, n (%)	21 (5.9)	34 (8.1)	10 (7.0)	11 (17.7)	0.014
Daytime SBP, mean (SD)	127.95 (10.14)	140.19 (10.34)	153.42 (12.69)	164.37 (15.47)	<0.001
Daytime DBP, mean (SD)	76.31 (9.37)	81.18 (10.83)	86.74 (12.25)	88.24 (12.07)	<0.001
Daytime PP, median ((IQR))	51 (45-57)	58 (52-66)	65 (58-73)	72 (62.25-86.25)	<0.001
Nighttime SBP, mean (SD)	109.48 (7.46)	128.19 (5.65)	147.12 (5.07)	171.52 (10.52)	<0.001
Nighttime DBP, mean (SD)	62.02 (7.34)	70.81 (8.24)	79.77 (9.59)	88.05 (12.85)	<0.001
Nighttime PP, median ((IQR))	47 (42-53)	57 (51-63)	68 (59-74.5)	84.5 (74-91)	<0.001
24 h SBP, mean (SD)	121.78 (9.33)	136.18 (8.61)	150.90 (9.27)	166.24 (12.66)	<0.001
24 h DBP, mean (SD)	71.57 (8.47)	77.69 (9.74)	84.41 (10.64)	88.10 (11.45)	<0.001
24 h PP, median ((IQR))	49 (45- 55)	58 (52-65)	66 (58-73)	74.5 (68-87)	<0.001
LVEF, median ((IQR))	68 (65-70)	69 (64.5-70)	68 (62.5-70)	67.5 [64-70)	0.387
IVS, mm; median ((IQR))	11 (10-12)	11 (10-12)	11.8 (10-12.75)	12 (11- 13)	<0.001
Daytime HTN, n (%)	87 (24.4)	297 (70.9)	134 (93.7)	61 (98.4)	<0.001
Treatment, n (%)	306 (85.7)	310 (74.0)	114 (79.7)	50 (80.6)	0.001
ACEI, n (%)	128 (35.9)	136 (32.5)	50 (35.0)	18 (29.0)	0.631
ARBs, n (%)	129 (36.1)	134 (32.0)	54 (37.8)	23 (37.1)	0.486
Calcium channel blockers, n (%)	92 (25.8)	106 (25.3)	42 (29.4)	16 (25.8)	0.812
Thiazides, n (%)	45 (12.6)	40 (9.5)	21 (14.7)	7 (11.3)	0.331
Aldosterone antagonist, n(%)	10 (2.8)	6 (1.4)	2 (1.4)	2 (3.2)	0.468
Beta-blocker, n (%)	105 (29.4)	88 (21.0)	45 (31.5)	18 (29.0)	0.018
Statins, n (%)	114 (31.9)	108 (25.8)	36 (25.2)	25 (40.3)	0.037
Aspirin, n (%)	66 (18.5)	65 (15.5)	24 (16.8)	7 (11.3)	0.467
CrCl, mean (SD)	106.35 (41.92)	111.92 (51.30)	111.57 (50.20)	111.73 (65.36)	0.417
MACE, n (%)	8 (2.2)	17 (4.1)	8 (5.6)	7 (11.3)	0.007
CV death, n (%)	8 (2.2)	15 (3.6)	7 (4.9)	5 (8.1)	0.102
Primary endpoint, n (%)	27 (7.6)	61 (14.6)	27 (18.9)	15 (24.2)	<0.001
Heart failure, n (%)	4 (1.1)	8 (1.9)	1 (0.7)	5 (8.1)	0.002
Hypertensive crisis, n (%)	9 (2.5)	27 (6.4)	14 (9.8)	3 (4.8)	0.007
Follow-up in months, median (IQR)	41 (28-54)	39 (24-53)	38 (18-49)	37 (18.50-47.75)	0.020

ACEI: angiotensin-converting enzyme inhibitors; ACS: acute coronary syndrome; AF: atrial fibrillation; ARBs: angiotensin II receptor blockers; BMI: body mass index; CrCl: creatinine clearance; CHF: Chronic heart failure; CV: cardiovascular; DBP: Diastolic blood pressure; HTN: hypertension; IQR: interquartile range; IVS: interventricular septum; LVEF, left ventricular ejection fraction; MACE: major adverse cardiovascular events; OSAHS: obstructive sleep apnea and hypopnea syndrome; PP: pulse pressure; SBP: systolic blood pressure; SD: standard deviation

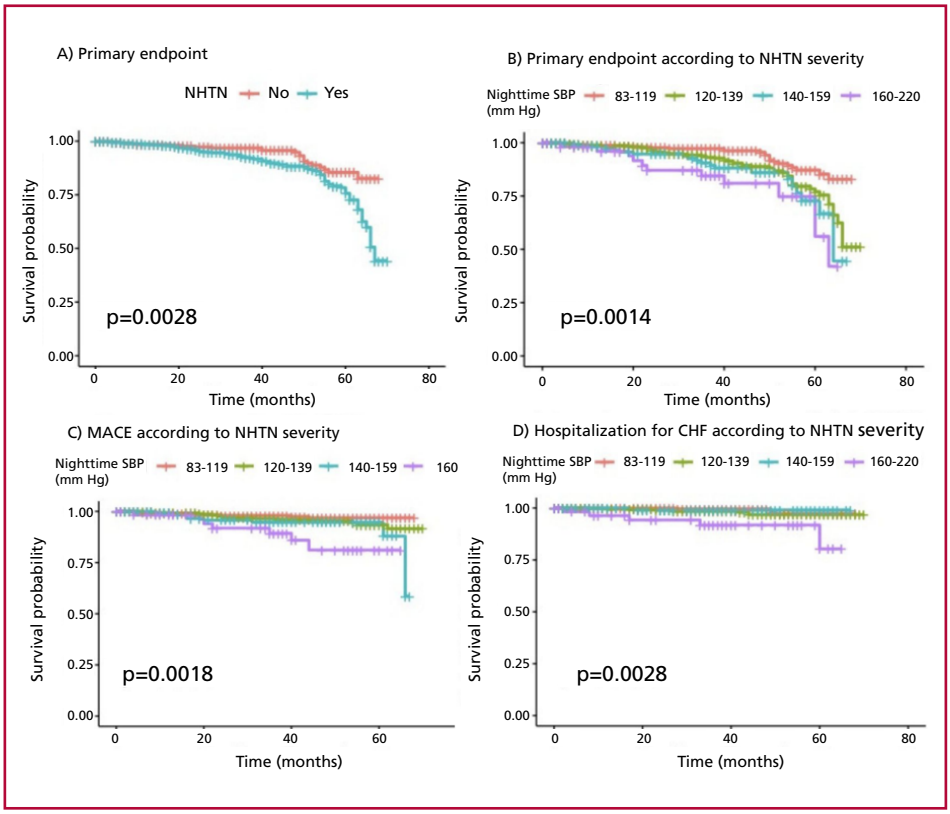

Fig. 1. Event-free survival. A) Primary endpoint according to the presence of nocturnal arterial hypertension (NHTN). B), C) and D) Primary endpoint, MACE and hospitalization for chronic heart failure (CHF) according to NHTN strata

SBP: systolic blood pressure

Table 2. Predictors of cardiovascular events. Bivariate analysis

Variable	b coefficient	HR (95% CI)	p
Diabetes	0.402	1.49 (0.72-3.09)	0.391
OSAHS	0.226	1.25 (0.44-3.49)	0.700
BMI			
Overweight	0.270	1.31 (0.58-2.91)	0.509
Obesity	0.485	1.62 (0.74-3.55)	0.223
NHTN stages			
120-139 mmHg	0.953	2.59 (1.25-5.36)	0.010
140-159 mmHg	0.869	2.38 (0.86-6.58)	0.090
160-220 mmHg	1.066	2.90 (0.99-8.51)	0.051
Age	0.020	1.02 (0.99-1.04)	0.072
LV hypertrophy	0.831	2.29 (1.28-4.12)	0.005
Patterns of HTN			
Attenuated dipper	0.199	1.22 (0.49-3.05)	0.674
Non-dipper	0.661	1.93 (0.87-4.29)	0.101
Inverted dipper	0.893	2.44 (0.97-6.12)	0.052
Hyper dipper	1.351	3.86 (1.68-8.88)	0.001
Smoking	0.981	2.67 (1.51-4.73)	0.001

BMI: body mass index; HR: hazard ratio; LV: left ventricular; NHTN: nocturnal hypertension; OSAHS: obstructive sleep apnea and hypopnea syndrome; 95% CI: 95% confidence interval.

Variable	b coefficient	HR (95% CI)	p
Model 1			
NHTN strata			
120-139 mmHg	1.110	3.03 (1.44-6.37)	0.003
140-159 mmHg	1.306	3.69 (1.36-10)	0.010
160-220 mmHg	1.907	6.73 (2.32-1.95)	<0.001
Age	0.03	1.03 (1-1.05)	0.006
LV hypertrophy	0.80	2.22 (1.24-3.98)	0.006
Daytime HTN	-0.30	0.73 (0.38-1.41)	0.356
Model 2			
NHTN strata			
120-139 mmHg	0.263	1.30 (0.65-2.58)	0.454
140-159 mmHg	0.811	2.25 (1.02-4.94)	0.041
160-220 mmHg	1.431	4.18 (1.60-10.8)	0.003
Age	0.039	1.04 (1.01-1.06)	<0.001
LV hypertrophy	0.858	2.35 (1.32-4.20)	0.003

HR: hazard ratio; HTN: hypertension; LV: left ventricle; NHTN: nocturnal hypertension

Table 3. Predictors of cardiovascular events. Multivariate analysis

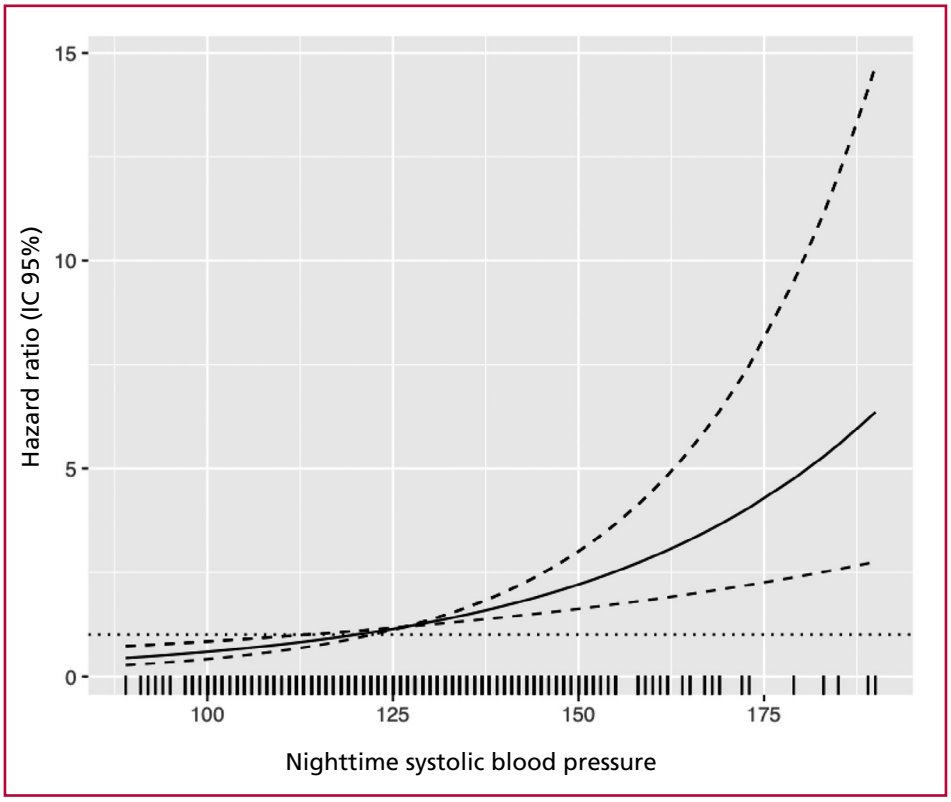

Fig. 2 Continuous association between nighttime systolic blood pressure and risk of cardiovascular events. Solid line represents the Hazard Ratio. Dashed lines represent the 95% confidence intervals. We can observe that the risk starts to increase from 127 mmHg

and it is possible that the prevalence of the NHTN phenotype is underestimated because its diagnosis depends on the request for 24-h pressure monitoring. (13) In our cohort, this prevalence was 69% and we were able to observe that these patients had a greater number of cardiovascular comorbidities and less antihypertensive treatment. In their work, also carried out in Argentina, Salazar et al (14) found a NHTN prevalence of 61%. Individuals with NHTN had greater history of previous cardiovascular disease (4.2% vs. 1.5%, p= 0.007). These authors found no differences in terms of classical cardiovascular risk factors or in relation to antihypertensive treatment. In another study by Yao Du et al. (15) the

reverse dipper or riser pattern was associated with a greater number of comorbidities, including renal dysfunction, overweight and diabetes. In addition to this, they were able to determine that those patients with NHTN presented a 77% higher risk (HR 1.77, 95% CI 1.25-2.50) compared with those without this condition.

Very few previous studies have studied NHTN according to its severity. (16) We were able to prove that the higher the level of nighttime blood pressure, the higher the risk of cardiovascular events. In addition, we were able to determine that this risk begins to increase very early and close to the reference value by which NHTN is defined (127 mmHg) (Figure 2). This is important, since it not only determines a goal to be achieved by antihypertensive treatment, but also reinforces the notion that nighttime blood pressure measurements carry valuable prognostic information.

Hypertension is an important and very frequent comorbidity in patients with a history of heart failure, especially in those with preserved left ventricular ejection fraction. From previous studies we know that more than 50% of patients with heart failure suffer from HTN. (17,18) In their study, Huang et al. in a cohort of patients with a previous diagnosis of heart failure with preserved ejection fraction showed prevalence of HTN in 77% of patients, 40% of which had NHTN. (19) These authors verified that the presence of NHTN is independently associated with rehospitalization for heart failure in the long-term follow-up. In another interesting study carried out by Kidawara et al (20) in patients with diabetes and without previous heart failure, the presence of NHTN behaved as an independent predictor of the progression of left ventricular diastolic dysfunction. In our cohort, as part of an exploratory analysis, we were able to observe a tendency to greater hospitalization for heart failure associated with the presence of NHTN, and that this risk is related to the severity of NHTN.

Our study has some limitations: first and foremost, the retrospective design, which implies biases. Although multivariate regression analysis was performed, we cannot completely rule out the possibility that variables may have altered our results. Secondly, this was a single-center study; however, it was a heterogeneous population with characteristics similar to those of previous studies. Thirdly, as this is a relatively healthy population, we believe that a larger sample size accompanied by a longer follow-up would allow us to determine with greater accuracy the impact of NHTN on cardiovascular events.

In conclusion, in this cohort of patients with HTN the NHTN phenotype and its severity were associated with adverse cardiovascular outcomes at the long-term follow-up.

Conflicts of interest

None declared.

(See authors' conflict of interests forms on the web).

Financing

None.

REFERENCES

1. Virani SS, Alonso A, Aparicio HJ, Benjamin EJ, Bittencourt MS, Callaway CW, et al. Heart disease and stroke statistics-2021 update: a report from the American Heart Association. Circulation 2021;143:e254-e743.

2. Goldsborough E 3rd, Osuji N, Blaha MJ. Assessment of Cardiovascular Disease Risk: A 2022 Update. Endocrinol Metab Clin North Am. 2022 ;51:483-509. doi: 10.1016/j.ecl.2022.02.005.

3. Fuchs FD, Whelton PK. High blood pressure and cardiovascular disease. Hypertenion. 2020;75:285-92. https://doi.org/10.1161/HYPERTENSIONAHA.119.14240

4. Leung AA, Nerenberg K, Daskalopoulou SS, McBrien K, Zarnke KB, Dasgupta K, et al; CHEP Guidelines Task Force. Hypertension Canada's 2016 Canadian Hypertension Education Program guidelines for blood pressure measurement, diagnosis, assessment of risk, prevention, and treatment of hypertension. Can J Cardiol 2016;32:569-88. https://doi.org/10.1016/j.cjca.2016.02.066.

5. Whelton PK, Carey RM, Aronow WS, Casey DE Jr, Collins KJ, Dennison Himmelfarb C, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/ NMA/PCNA guideline for prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol 2018;71(19):e127-e248. https://doi.org/10.1016/j.jacc.2017.11.006.

6. National Institute for Health and Clinical Excellence (NICE). Hypertension in adults: diagnosis and management. Published August 2011. Updated November 2016. Accessed June 3, 2019.

7. Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M, et al; ESC Scientific Document Group. 2018 ESC/ESH Guidelines for the management of arterial hypertension. Eur Heart J 2018;39:3021-104. https://doi.org/10.1093/eurheartj/ehy339.

8. Dolan E, Stanton A, Thijs L, Hinedi K, Atkins N, McClory S, et al. Superiority of ambulatory over clinic blood pressure measurement in predicting mortality: the Dublin outcome study. Hypertension 2005;46:156–61. https://doi.org/10.1161/01.HYP.0000170138.56903.7a

9. Sega R, Facchetti R, Bombelli M, Cesana G, Corrao G, Grassi G, et al. Prognostic value of ambulatory and home blood pressures compared with office blood pressure in the general population: follow- up results from the Pressioni Arteriose Monitorate e Loro Associazioni (PAMELA) study. Circulation 2005;111:1777–83. https://doi.org/10.1161/01.CIR.0000160923.04524.5B

10. Hansen TW, Jeppesen J, Rasmussen S, Ibsen H, Torp-Pedersen C. Ambulatory blood pressure and mortality: a population- based study. Hypertension 2005;45:499–504. https://doi.org/10.1161/01.HYP.0000160402.39597.3b

11. Unger T, Borghi C, Charchar F, Khan NA, Poulter NR, Prabhakaran D, et al. 2020 International Society of Hypertension Global Hypertension Practice Guidelines. Hypertension 2020 ;75:1334-57. https://doi.org/10.1161/HYPERTENSIONAHA.120.15026.

12. Tang F, Ishwaran H. Random Forest Missing Data Algorithms. Stat Anal Data Min 2017;10:363-77. https://doi.org/10.1002/sam.11348.

13. Kreutz R, Brunström M, Burnier M, Grassi G, Januszewicz A, Muiesan ML. et al. European Society of Hypertension clinical practice guidelines for the management of arterial hypertension. Eur Intern Med 2024;126:1-15. https://doi.org/10.1016/j.ejim.2024.05.033.

14. Salazar MR, Espeche WG, Balbin E, Leiva Sisnieguez CE, Minetto J, Leiva Sisnieguez BC, et al. Prevalence of isolated nocturnal hypertension according to 2018 European Society of Cardiology and European Society of Hypertension office blood pressure categories. J Hypertens 2020;38:434-40. https://doi.org/10.1097/

HJH.0000000000002278.
15. Du Y, Zhu B, Liu Y, Zhou W, Du Z, Yang W, et al. Association between nocturnal blood pressure phenotype and adverse cardiovascular prognosis in patients with coronary heart disease and hypertension. J Clin Hypertens 2024;26:405-15. https://doi.org/10.1111/jch.14790
16. Yang W, Y, Melgarejo JD, Thijs L, Zhang ZY, Boggia J, Wei FF, et al. Association of Office and Ambulatory Blood Pressure With Mortality and Cardiovascular Outcomes. JAMA 2019:332:409-20. https://doi.org/10.1001/jama.2019.9811.
17. Bhatia RS, Tu JV, Lee DS, Austin PC, Fang J, Haouzi A, et al. Outcome of heart failure with preserved ejection fraction in a population-based study. N Engl J Med 2006;355:260-9. https://doi.org/10.1056/NEJMoa051530
18. Yancy CW, Lopatin M, Stevenson LW, De Marco T, Fonarow GC; ADHERE Scientific Advisory Committee and Investigators. Clinical presentation, management, and in-hospital outcomes of pati- ents admitted with acute decompensated heart failure with preserved systolic function: a report from the Acute Decompensated Heart Failure National Registry (ADHERE) Database. J Am Coll Cardiol 2006;47:76-84.
19. Huang G, Liu XH, Zhang Y, Zhu YX, He Y, Wang TB, et al. Nocturnal hypertension and riser pattern are associated with heart failure rehospitalization in patients with heart failure with preserved ejection fraction. J Geriatr Cardiol 2023;20:448-58. https://doi.org/10.26599/1671-5411.2023.06.003
20. Kidawara Y, Kadoya M, Igeta M, Morimoto A, Miyoshi A, Kakutani-Hatayama M,et al. Nocturnal Hypertension and Left Ventricular Diastolic Dysfunction in Patients With Diabetes With the Absence of Heart Failure: Prospective Cohort HSCAA Study Hypertension. 2024;81:172–82. https://doi.org/10.1161/HYPERTENSIONAHA.123.21304