ORIGINAL PAPER

Reproducibility study of nocturnal blood pressure dipping in patients with high cardiovascular risk

Natalia Burgos-Alonso PhD^{1,2} | Maria Victoria Ruiz Arzalluz MD^{1,3} | Arturo Garcia-Alvarez MSc¹ | Daniel Fernandez-Fernandez de Quincoces MSc¹ | Gonzalo Grandes MD¹

¹Primary Care Research Unit of Bizkaia, BioCruces Bizkaia Health Research Institute, Bilbao, Spain

²Preventive Medicine and Public Health Department, Faculty of Medicine and Nursery. University of the Basque Country (UPV/EHU), Bilbao, Spain

³Tolosaldea Health Region, Basque Health Service (Osakidetza), Bilbao, Spain

Correspondence

Natalia Burgos-Alonso, Unidad de Investigación de Atención Primaria Osakidetza, Luis Power 18, 4a planta. E-48014 - Bilbao, Spain. Email: natalia.burgos@ehu.es

Funding information A grant was received from the Department of Pharmacy of the Spanish Health Ministry.

Abstract

It has been shown that in most people there is a physiological reduction in blood pressure during nighttime sleep, it falling by approximately 10% compared to daytime values (dippers). On the other hand, in some people, there is no nighttime reduction (non-dippers). Various studies have found an association between being a non-dipper and a higher risk of cardiovascular disease, but few have assessed whether the nocturnal pattern is maintained over time. From the database of the TAHPS study, data were available on 225 patients, each of whom underwent 24-hour ambulatory blood pressure monitoring (ABPM) on four occasions over a period of 5 months. We studied the reproducibility of the nocturnal BP dipping pattern with mixed linear analysis and also calculated the concordance in the classification of patients as dippers or non-dippers. The intraclass correlation coefficients between the different ABPM recordings were 0.482 and 0.467 for systolic and diastolic blood pressure, respectively. Two-thirds (67%) and 70% of the patients classified, respectively, as dippers or non-dippers based on systolic and diastolic blood pressure readings in the first ABPM recording were found to have the same classification based on the subsequent recordings. We conclude that the reproducibility of nocturnal dipping patterns and concordance of dipper vs non-dipper status in individual patients is modest and therefore that we should be cautious about recommending treatments or interventions based on these patterns.

1 | INTRODUCTION

Ambulatory blood pressure monitoring (ABPM) allows us to measure blood pressure (BP) values and heart rate for periods of 24 and even 48 hours while people go about their normal daily activities. For this reason, this approach is extremely useful for confirming a diagnosis of hypertension, as well as for monitoring the response to antihypertensive treatment.¹⁻³

Values of BP measured using ABPM are more strongly correlated with target organ damage and have greater prognostic value for cardiovascular events than those measured in the consultation room.⁴ Further, this type of monitoring provides data on circadian changes in BP, such as decreases during sleep, which are of great importance as prognostic factors.⁵

It has been shown that in most people there is a physiological reduction in BP during nighttime sleep, it falling by approximately 10%

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made. © 2021 The Authors. The Journal of Clinical Hypertension published by Wiley Periodicals LLC

compared to daytime values (dippers). On the other hand, in some people, it falls by more than 20% (extreme dippers), while in some there is no nighttime reduction (non-dippers), and in others, BP does not fall but rather increases (risers).⁶

Some studies have demonstrated that non-dippers and especially risers have an elevated risk of cardiovascular disease and are more likely to have target organ damage.^{5,7-13} A meta-analysis published in 2019 analyzing 17 312 patients with hypertension concluded that, regardless of 24-hour BP levels, the nocturnal BP pattern is predictive of cardiovascular events, non-dipper individuals and especially risers having a poorer prognosis. On the other hand, being an extreme dipper appeared to be protective in patients with treated hypertension, but not in untreated patients.¹⁴

Nonetheless, several studies have suggested that when the ABPM is repeated after some time, dipper vs non-dipper status is only moderately reproducible.¹⁵⁻¹⁷ There is a scarcity of studies on reproducibility, and however, and most that have been published are based on data from two ABPM recordings and mixed populations of patients with treated and untreated hypertension and with or without target organ damage.^{15,18-20} This explains why scientific societies have yet to state what therapeutic approach they consider most appropriate in such patients.

In this study, we assessed the reproducibility of the circadian BP pattern in a population of patients with medically treated hypertension and a history of cardiovascular events who underwent ABPM on four occasions.

2 | MATERIALS AND METHODS

We conducted a study on nocturnal BP dipping. For this, we calculated the nocturnal BP fall expressed as a percentage of the daytime BP ((daytime BP – nighttime BP)/daytime BP)*100) to classify participants as dippers (a decrease of \geq 10% or more of blood pressure at night) or non-dippers.

Data were obtained as part of the Effectiveness of Night Administration of Low Dose Aspirin in Hypertensive Patients (TAHPS) study (ClinicalTrial.gov identifier, NCT01741922), approved by the Clinical Research Ethics Committee of Euskadi (Ref: 115/2011). This clinical trial assessed whether acetylsalicylic acid (ASA) at low doses taken at bedtime had an effect on BP or nocturnal fall in BP and concluded that the time when ASA was taken did not have an effect on patients' BP or the dipper/non-dipper pattern.²¹

The population was 225 patients on antihypertensive therapy and low doses of ASA for secondary prevention of cardiovascular disease. Data were collected in 20 health centers in Bizkaia, Gipuzkoa and Barcelona, between 1 November 2011 and 31 December 2015. The systolic and diastolic BP was measured every 20 min between 07:00 and 23:00 and every 30 min between 23:00 and 07:00 in all patients. These times were used to define/calculate the mean daytime and mean nighttime BP levels. We used the WatchBP® ABPM device in all centers. For data from a given ABPM recording to be included, it was required that there were no more than 2 consecutive hours with no readings and at least 70% of readings were considered valid. As there may be a potential loss in external validity or generality using this restrictive criteria, we perform a sensitivity analysis using the International Database of Ambulatory Blood Pressure in Relation to Cardiovascular Outcome [IDACO] criteria²² (≥10 daytime and ≥ 5 nighttime readings).

Patients included were adults with a high risk of cardiovascular events whose treatment for hypertension had not been changed within 6 months before the study. On the other hand, patients were excluded if they were shift workers; on long-term NSAID therapy, anticoagulants or antiplatelet agents, or ASA at doses other than 100-150 mg; heavy drinkers (>280 g/week in men and 170 g/week in women) or women who were pregnant or breastfeeding; or if they had any serious or terminal disease, NYHA class III heart failure, glomerular filtration < 45 ml/min, or any physical or mental condition that might hinder their collaboration.

Patients were recruited at random, by the research unit using a computer program to randomly select patients who a priori met the criteria based on coded data and doctors then contacting patients in the order they appeared the list provided by the research unit. At the first visit, doctors confirmed, by taking a medical history, that the selected patients met all the inclusion criteria and none of the exclusion criteria. They then invited them to participate in the study and, having informed them about the research, asked them to give written informed consent. If any patients had their antihypertensive therapy changed or its dose or regime modified, they were excluded from the analysis. The first ABPM recording was performed at recruitment and the following recordings 2, 3, and 5 months later.

The primary objective of this study was to assess the real reproducibility of the nocturnal fall in BP as a percentage of the daytime value ((daytime BP – nighttime BP)/daytime BP)*100) observed in the patient's first ABPM recording, which was the information that would normally be available when they were seen, compared to the percentage fall obtained from subsequent recordings and to the mean value. Further, we studied the agreement in the classification of the dipper pattern between measurements, including an aggregate measure in which patients are considered to be dippers when the mean percentage fall in the three subsequent recordings was \leq 10%.

As a secondary objective, we analyzed whether the reproducibility was higher or lower in various subgroups of the population (>70-year-olds and patients with diabetes, obesity, or hypertension).

2.1 | Statistical analysis

To analyze the reproducibility of the nocturnal pattern, we used various different approaches. On the one hand, exploiting the fact that we had four measurements per patient, we calculated intraclass correlation coefficients (ICCs) for the percentage fall using two-level (recording and patient) linear mixed models. The ICC measures the

1042

WILEY

correlation between measurements in a given patient, estimating the fraction of the variance that corresponds to differences between measurements in the same patient compared to those between measurements in different patients.

On the other hand, we followed the strategy of Bland and Altman ²³ which involves calculating Pearson's correlation coefficients and Bland-Altman repeatability coefficients between the first recording and the others as well as the means.

The percentage repeatability coefficients, defined as the ratio of the within-person standard deviation to the between-person standard deviation, were obtained by dividing the standard deviation of the differences between pairs of repeated measurements by two times the pooled standard deviation of the measurements and multiplying the result by 100.²⁴ Because the repeatability coefficient is the inverse of the reproducibility, a high repeatability coefficient indicated a low reproducibility and vice versa.

Further, to assess the reproducibility of the classification of patients as dippers or non-dippers, we have calculated the level of concordance (percentage of patients whose classification remained unchanged) between two measurements and the corresponding Kappa statistics.

All the analyses were performed in SAS (vs 9.4) and R.

TABLE 1 Baseline characteristics

3 | RESULTS

A total of 225 patients were included of which 206 completed the second recording, 200 the third and 192 the last recording. The ABPM data were considered invalid in 11, 21, 20, and 27 cases at the time of the first, second, third, and fourth recordings, respectively. Giving a total of 214, 185, 180, and 165 valid ABPM measurements at each recording. During the study, 140 patients had valid ABPM in all recordings. Table 1 summarizes the baseline characteristics of the 225 patients included in the study. According to the first recording, 48.1% of the patients were dippers based on their systolic blood pressure (SBP) and 64.5% based on their diastolic blood pressure (DBP).

3.1 | Reproducibility of the day-to-night change in BP

Analyzing the percentage fall in BP across the four recordings, we obtained ICCs of 0.482 for SBP and 0.467 for DBP, indicating that the variance in measurements taken in the same patient (ie, the variance due to the inconsistency or lack of reproducibility) is slightly more than half the variance in measurements taken in different patients.

	Sample size		Mean		Standard dev	/iation
SBP, mm Hg	214		125.55		11.62	
DBP, mm Hg	214		70.62		6.94	
Nocturnal fall in SBP (% of daytime value)	214		8.66		9.01	
Nocturnal fall in DBP (% of daytime value)	214		12.59		9.96	
Age, years	225		68.24		9.19	
Body mass index, kg/m ²	224		29.16		3.94	
				N		%
SBP dippers (including extreme dippers)		214		103		48.1
DBP dippers (including extreme dippers)		214		138		64.5
Female		225		67		29.8
Smokers		222		22		9.9
Diabetes		222		80		36.6
Heart disease		222		145		65.3
Chronic obstructive pulmonary disease		222		20		9
Arterial disease		222		41		18.5
Congestive heart failure		222		5		2.2
Stroke		222		55		24.8
Dyslipidemia		222		147		66.2
Statins		222		178		80.2
Enzyme inhibitors		222		170		76.6
Calcium antagonists		222		58		26.1
Beta-blockers		222		83		37.4

Abbreviations: DBP, Diastolic blood pressure; SBP, Systolic blood pressure.

Figure 1 illustrates the relationship between the percentage fall in BP measured in the first and subsequent ABPM recordings. The strength of the linear correlation decreases the further in time the subsequent recording is from the first, changing from r = 0.52/0.48(SBP/DBP) comparing the baseline recording with that at 2 months, to r = 0.42/0.41 comparing with that at 5 months (see Table 2), and is higher when comparing the first recording with the mean of the three subsequent ones (r = 0.55/0.5). Table 2 shows how this pattern is also seen on analyzing the repeatability coefficients, with slightly better reproducibility (lower repeatability coefficient) for SBP than DBP.

3.2 | Reproducibility of the dipper vs non-dipper classification

From the results in Table 3, it can be seen that the percentage of patients whose classification did not change from that assigned after the first ABPM recording was never higher than 72%. All the kappa coefficients except one are below the 0.40 mark which indicates poor agreement. The reproducibility was slightly better for DBP than SBP.

Analyzing the reproducibility considering the extreme patterns, we found that 10%/23% of patients classified as risers (with a negative percentage fall, ie, BP being higher at night than in the day) after the first recording (n = 37 for SBP and 21 for DBP) were classified as dippers based on SBP/DBP considering the three subsequent recordings. Further, among patients classified as extreme dippers (percentage fall > 20%) at the first recording (n = 21/43), 14%/16% were subsequently classified as non-dippers.

3.3 | Reproducibility in subgroups

Analyzing the circadian pattern in different subgroups of the study population, we observed that the reproducibility of day to night change in BP was poorer in patients with diabetes (ICC: 0.434/0.343 SBP/DBP) and in those with obesity (body mass index > 30 kg/m²) (ICC: 0.324/0.339) and better in patients who had high daytime SBP at the first recording (>135 mmHg) (ICC: 0.562/0.604) as well as in over 70-year-olds (CCI: 0.581/0.518) (Appendix).

3.4 | Sensitivity analysis

Using the IDACO criteria, ABPM data were considered valid in 224, 199, 199, and 187 cases at the time of the first, second, third, and

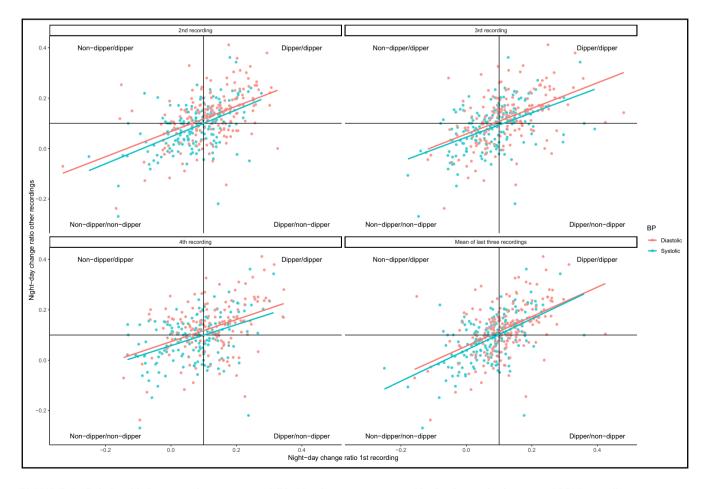


FIGURE 1 Relationship between the percentage fall in blood pressure measured in the first and subsequent ABPM recordings

TABLE 2 Reproducibility of the day-to-night percentage change in BP

Nocturnal fall in blood pressure (% of daytime value)	SBP					DBP				
	Mean	Sd	ICC	Correlation	Repeatability	Mean	Sd	ICC	Correlation	Repeatability
1st recording	8.66	9.02	0.482			12.6	9.96	0.467		
2nd recording	7.69	8.56		0.515	48.9	11.9	9.69		0.487	50.6
3rd recording	8.1	9.22		0.485	50.6	12.8	9.66		0.476	51.5
4th recording	7.33	9.32		0.418	54.9	12	9.75		0.412	55.4
Mean	7.47	8.06		0.549	47.5	12.1	8.61		0.5	49.9

Abbreviations: DBP, Diastolic blood pressure; ICC, Intraclass correlation coefficient; SBP, Systolic blood pressure; SD, Standard deviation.

fourth recordings, respectively. Using these data, we observed a modest improvement in the reproducibility of day to night change in BP (ICC: 0.512/0.483 SBP/DBP) and dipper classification (Appendix) respect to the results with the more restrictive criteria.

4 | DISCUSSION

Since devices for ABPM have been available and it has been known that BP follows a circadian pattern with a nocturnal fall, numerous studies have been performed showing that the lack of such a dip (non-dipper or riser patterns) is associated with a significantly higher risk of cardiovascular events.²⁵⁻²⁸

For this reason, it is essential to know how reproducible this pattern is, but nonetheless, this question has been poorly studied. Specifically, the studies carried out to date have not reported more than two ABPM recordings.^{18,29-31} In contrast, we report data from 225 patients who underwent ABPM on four occasions over a period of 5 months. During this study period, no changes in antihypertensive therapy or the time of its administration were allowed, this being closely monitored. All patients received treatment for hypertension and ASA 100 mg as an antiplatelet agent given their diagnosed high blood pressure and a history of cardiovascular events.

We believe, therefore, that this is the first study reporting four ABPM recordings for each individual in a homogeneous controlled group, this enabling us to study the reliability of the dipper pattern in this type of patient, not only by repeating the ABPM but by checking the classification over four ABPM recordings. We found that for both SBP and DBP the variation in nocturnal fall between different measurements in the same patient, which ideally would be very low, is about half that of the variation between measurements in different patients, indicating a low or at most modest reproducibility. These findings are confirmed on analyzing Pearson's correlation coefficients and reproducibility coefficients which were only higher than 0.5 and lower than 0.4 in a few cases. This yields concordance values very similar to those in the study of Ben-DOV et al ³² who obtained Pearson's r of 0.52 for reproducibility of the SBP pattern.

Except in the case of comparing baseline DBP with that at 4 months (71.8%), the concordance in the classification of the dipper pattern between measurements is no higher than 70% and even considering those classified as extreme dippers or risers the pattern may change. Previous publications have reported figures for reproducibility that are similar to those found in our study or slightly lower.^{29,31,33} Omboni et al observed a reproducibility of 60.3% considering SBP and 60.9% considering DBP.¹⁸

Gorostidi et al³⁴ and at Booth et al study³⁵ noted that the nondipper pattern is more common and the reproducibility is slightly higher in high-risk patients than in other groups. Given that the patients in the TAHPS study had high cardiovascular risk and 52% of them were non-dippers, we expected to find better reproducibility than in the aforementioned studies. Nonetheless, the values we found are not much higher, though we did find better reproducibility in patients who had high daytime SBP (>135 mm Hg).

It has also been reported that the reproducibility of the non-dipper pattern is better in patients with diabetes than in the other patients with hypertension,²⁸ but in our study, the reproducibility in patients with diabetes was actually lower than in the overall study population.

As a limitation of our study, we should recognize that it involves patients with hypertension and high cardiovascular risk, and hence, the findings cannot be extrapolated to other populations. On the other

TABLE 3	Reproducibility of the	dipper vs non-dipper	classification

	SBP				DBP	DBP				
Dippers	n	%	Agreement (%)	Карра	n	%	Agreement (%)	Карра		
1st recording	103	48.1			138	64.5				
2nd recording	77	41.6	65.9	0.31	116	62.7	68.2	0.31		
3rd recording	68	37.8	68.4	0.34	108	60	71.8	0.41		
4th recording	63	38.2	57.9	0.15	96	58.2	63.5	0.24		
Mean	69	34	67.3	0.34	123	60.6	69.9	0.36		

Abbreviations: DBP, Diastolic blood pressure; SBP, Systolic blood pressure.

└WILEY

1046

hand, it is precisely in this population that we are interested in reducing cardiovascular risk and optimizing treatments. Another limitation is that we opted for a fixed timetable for the sleep/wake period and did not take into account daytime naps. Nonetheless, research related to this issue has not detected differences in reproducibility related to the day/night pattern or approach to delimiting the sleep period.³⁶

5 | CONCLUSIONS

This study, based on 225 patients each of whom underwent ABPM on four occasions, confirms the modest reproducibility of circadian BP patterns, and therefore, we should be cautious about initiating or modifying treatments based on these patterns, above all if ABPM is only performed once.

Nonetheless, there is evidence that the non-dipper pattern is associated with a higher cardiovascular risk, and hence, there is a need for further research to develop methods allowing us to establish circadian BP patterns more reliably.

ACKNOWLEDGEMENTS

TAHPS Group: Ernest Vinyoles, Maria Cruz Gomez Ruiz, Monika Salgueiro Macho, Rosa Morros Pedros, Helena Pera Pujadas, Anna Garcia Sangenis, M^a Jose Oyarbide Mondaluce, M^a Luz Rodríguez Ibáñez, Ricardo San Vicente Blanco, Mikel Lugue Jiménez, Maria Jesus Arzuaga Arambarri, Nerea Alonsotegi Larrinaga, Marta Cobos Rozadilla, Arritxu Zialtzeta Aduriz, Amaia Aguirre Azpiazu, Maria Jose Garcia Gil, Remedios Vega Iñigo, Santiago Ayechu Redín, Oihana Ezkurra Galdos, Jose Francisco Egido Arroyo, Iosune Alberdi Buruaga, M^a Jesus Bernaras Iturrioz, Amaia Arruti Querejeta, Juan Carlos Marlasca García, Ana Teresa Martínez Rementería, Loreto Palacio Elua, Violeta Gonzalez Urcelay, Itziar Hernando Mendibil, Mª Carmen Gonzalez Temprano, Julián Bajo García, Jose Antonio Quindimil Vázquez, Jose Félix Zuazagoita Nubla, Mª Teresa Amondarain Arratibel, M^a Dolores Marin Vicuña, Idoia Larrañaga Cortabarria, Magdalena Cuesta Ortiz, Kizkitza Alustiza Arteaga, Maria Carmen AraneguiLasue, Ane Marin Lacarta, Amaia Telleria Astarloa, Maria Luisa Garcia Aramaio, Elena Lizaso Guerrico, Josune Madariaga Jurrebaso, Mercedes Armendáriz Múgica, Ana Roncero Gascón, Mª Soledad Romera Alegría, Ana OrmaetxeMerodio, Azucena Ruiz Meléndez, Maria Aranzazu Anza Asurmendi, Mª Teresa González Sanchoyerto, María Mercedes Dolores Ferreras Castrillo, Mencía Benitez Camps, Jordi Ingla Más, Xavier Cos Claramunt, Jose Manuel Escudero Ibánez, Antonio Negrete Palma, August Huertas Campistol Carolina Guiriguet Capdevila, Mª Rosa Benedicto Acebo, Eva Acerboni Flores, and Francisco Barrio Torrell.

CONFLICT OF INTEREST

We declare no competing interests.

AUTHOR CONTRIBUTIONS

Maria Victoria Ruiz Arzalluz and Gonzalo Grandes conceived the idea and are the study guarantors. They were responsible for the study design and planningand obtained funding. Natalia Burgos Alonso was responsible for project coordination and supervision, analysis, and interpretation of results, and manuscript preparation. Arturo Garcia Alvarez and Daniel Fernandez Fernandez de Quincoces were in charge of performing the analysis of results and critically reviewed the manuscript. All contributors have approved this version submitted for publication to Journal of Clinical Hypertension.

DATA AVAILABILITY STATEMENT

The TAHPS study data are available only to the collaborating scientists from the respective TAHPS participating centers. The data may be available upon request for some of the participating centers but not for all due to relevant data protection laws.

ORCID

Natalia Burgos-Alonso D https://orcid.org/0000-0001-7230-3340

REFERENCES

- JCS Joint Working Group. Guidelines for the Clinical Use of 24 Hour Ambulatory Blood Pressure Monitoring (ABPM) (JCS 2010). *Circ J.* 2012;76(2):508-519.
- Myers MG. Ambulatory blood pressure monitoring for routine clinical practice. *Hypertension*. 2005;45(4):483-484.
- Pickering TG, Shimbo D, Haas D. Ambulatory blood-pressure monitoring. N Engl J Med. 2006;354(22):2368-2374.
- Mancia G, Di Rienzo M, Parati G, Grassi G. Sympathetic activity, blood pressure variability and end organ damage in hypertension. J Hum Hypertens. 1997;11(suppl 1):S3-8.
- 5. Mancia G, Parati G. Ambulatory blood pressure monitoring and organ damage. *Hypertension*. 2000;36(5):894-900.
- Mancia G, Fagard R, Narkiewicz K, et al. 2013 ESH/ESC Guidelines for the management of arterial hypertension: the Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). J Hypertens. 2013;31(7):1281-1357.
- Fagard RH, Celis H, Thijs L, et al. Daytime and nighttime blood pressure as predictors of death and cause-specific cardiovascular events in hypertension. *Hypertension*. 2008;51(1):55-61.
- Fagard RH, Thijs L, Staessen JA, Clement DL, De Buyzere ML, De Bacquer DA. Night-day blood pressure ratio and dipping pattern as predictors of death and cardiovascular events in hypertension. J Hum Hypertens. 2009;23(10):645-653.
- Kikuya M, Ohkubo T, Asayama K, et al. Ambulatory blood pressure and 10-year risk of cardiovascular and noncardiovascular mortality. *Hypertension*. 2005;45(2):240-245.
- 10. Zhang J, Wen R, Yin J, et al. Nocturnal pulse rate correlated with ambulatory blood pressure and target organ damage in patients with chronic kidney disease. *J Clin Hypertens (Greenwich, Conn)*. 2019;21(1):77-87.
- Li S, Wang X, Zhao L, et al. The characteristics of 24-hour ambulatory blood pressure monitoring and its relationship with cardiovascular target organ damage in Chinese Han patients with concomitant type 2 diabetes and hypertension. *Blood Press Monit.* 2019;24(4):167-173.
- 12. Bello NA, Jaeger BC, Booth JN 3rd, et al. Associations of awake and asleep blood pressure and blood pressure dipping with abnormalities of cardiac structure: the Coronary Artery Risk Development in Young Adults study. J Hypertens. 2020;38(1):102–110.
- Gong S, Liu K, Ye R, Li J, Yang C, Chen X. Nocturnal dipping status and the association of morning blood pressure surge with subclinical target organ damage in untreated hypertensives. *J Clin Hypertens* (Greenwich, Conn). 2019;21(9):1286-1294.

- Salles GF, Reboldi G, Fagard RH, et al. Prognostic Effect of the Nocturnal Blood Pressure Fall in Hypertensive Patients: The Ambulatory Blood Pressure Collaboration in Patients With Hypertension (ABC-H) Meta-Analysis. *Hypertension*. 2016;67(4):693-700.
- Hernandez-del Rey R, Martin-Baranera M, Sobrino J, et al. Reproducibility of the circadian blood pressure pattern in 24-h versus 48-h recordings: the Spanish Ambulatory Blood Pressure Monitoring Registry. J Hypertens. 2007;25(12):2406-2412.
- Hinderliter AL, Routledge FS, Blumenthal JA, et al. Reproducibility of blood pressure dipping: relation to day-to-day variability in sleep quality. J Am Soc Hypertens. 2013;7(6):432-439.
- McGowan NJ, Gough K, Padfield PL. Nocturnal dipping is reproducible in the long term. *Blood Press Monit.* 2009;14(5):185-189.
- Omboni S, Parati G, Palatini P, et al. Reproducibility and clinical value of nocturnal hypotension: prospective evidence from the SAMPLE study. Study on Ambulatory Monitoring of Pressure and Lisinopril Evaluation. J Hypertens. 1998;16(6):733-738.
- Palatini P, Mormino P, Canali C, et al. Factors affecting ambulatory blood pressure reproducibility. Results of the HARVEST Trial. Hypertension and Ambulatory Recording Venetia Study. *Hypertension*. 1994;23(2):211-216.
- Morrin NM, Stone MR, Henderson KJ. Reproducibility of 24-h ambulatory blood pressure and measures of autonomic function. *Blood Press Monit.* 2017;22(3):169-172.
- Ruiz-Arzalluz MV, Fernandez MC, Burgos-Alonso N, Vinyoles E, San Vicente Blanco R, Grandes G. Protocol for assessing the hypotensive effect of evening administration of acetylsalicylic acid: study protocol for a randomized, cross-over controlled trial. *Trials*. 2013;14(1):236.
- Thijs L, Hansen TW, Kikuya M, et al. The International Database of Ambulatory Blood Pressure in relation to Cardiovascular Outcome (IDACO): protocol and research perspectives. *Blood Press Monit*. 2007;12(4):255-262.
- Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet (London, England)*. 1986;1(8476):307-310.
- Staessen J, Bulpitt CJ, O'Brien E, et al. The diurnal blood pressure profile. A population study. Am J Hypertens. 1992;5(6 Pt 1):386-392.
- Schillaci G, Battista F, Settimi L, Schillaci L, Pucci G. Antihypertensive drug treatment and circadian blood pressure rhythm: a review of the role of chronotherapy in hypertension. *Curr Pharmaceutical Design*. 2015;21(6):756-772.
- 26. Sousa F, Neves J, Ferreira R, Polonia J, Bastos JM. 1B.05: in hypertension the change from a non-dipper to a dipper pattern is associated with a better cardiovascular prognosis than the persistence within the non-dipper pattern. J Hypertens. 2015;33(Suppl 1):e6.

- 27. Mahabala C, Kamath P, Bhaskaran U, Pai ND, Pai AU. Antihypertensive therapy: nocturnal dippers and nondippers. Do we treat them differently? *Vasc Health Risk Manag.* 2013;9:125-133.
- Ayala DE, Moya A, Crespo JJ, et al. Circadian pattern of ambulatory blood pressure in hypertensive patients with and without type 2 diabetes. *Chronobiol Int.* 2013;30(1–2):99-115.
- 29. Ash GI, Walker TJ, Olson KM, et al. Reproducibility of ambulatory blood pressure changes from the initial values on two different days. *Clinics (Sao Paulo, Brazil)*. 2013;68(12):1509-1515.
- Cuspidi C, Meani S, Valerio C, et al. Reproducibility of dipping/ nondipping pattern in untreated essential hypertensive patients: impact of sex and age. *Blood Press Monit*. 2007;12(2):101-106.
- Bo Y, Kwok KO, Chung VC, et al. Short-term reproducibility of ambulatory blood pressure measurements: a systematic review and meta-analysis of 35 observational studies. J Hypertens. 2020;38(11):2095-2109.
- Ben-Dov IZ, Ben-Arieh L, Mekler J, Bursztyn M. Blood pressure dipping is reproducible in clinical practice. *Blood Press Monit*. 2005;10(2):79-84.
- Felicio JS, Pacheco JT, Ferreira SR, et al. Reproducibility of ambulatory blood pressure monitoring in hypertensive patients with type 2 diabetes mellitus. Arquivos Bras Cardiol. 2007;88(2):206-211.
- Gorostidi M, Sobrino J, Segura J, et al. Ambulatory blood pressure monitoring in hypertensive patients with high cardiovascular risk: a cross-sectional analysis of a 20,000-patient database in Spain. J Hypertens. 2007;25(5):977-984.
- 35. Booth JN 3rd, Muntner P, Abdalla M, et al. Differences in nighttime and daytime ambulatory blood pressure when diurnal periods are defined by self-report, fixed-times, and actigraphy: Improving the Detection of Hypertension study. J Hypertens. 2016;34(2):235-243.
- Dimsdale JE, von Kanel R, Profant J, Nelesen R, Ancoli-Israel S, Ziegler M. Reliability of nocturnal blood pressure dipping. *Blood Press Monit*. 2000;5(4):217-221.

How to cite this article: Burgos-Alonso N, Ruiz Arzalluz MV, Garcia-Alvarez A, Fernandez-Fernandez de Quincoces D, Grandes G. Reproducibility study of nocturnal blood pressure dipping in patients with high cardiovascular risk. *J Clin Hypertens*. 2021;23:1041–1050. <u>https://doi.org/10.1111/</u> jch.14222

APPENDIX 1

Results using the IDACO criteria

Nocturnal fall in blood	SBP	SBP					DBP				
pressure (% of daytime value)	Mean	SD	ICC	Correlation	Repeatability	Mean	SD	ICC	Correlation	Repeatability	
1st recording	7.3	7.68	0.434			11.1	8.47	0.343			
2nd recording	7.6	7.43		0.508	47.1	10.8	7.95		0.461	49.3	
3rd recording	6.22	9.34		0.604	45.1	11.6	8.78		0.534	49.1	
4th recording	5.51	8.92		0.337	58.3	11.2	9.09		0.193	63.7	
Mean	6.11	7.4		0.629	43.4	10.9	6.9		0.488	50.3	

TABLE 1 Reproducibility of the day-to-night percentage change in BP in patients with diabetes

Abbreviations: DBP, Diastolic blood pressure; ICC, Intraclass correlation coefficient; SBP, Systolic blood pressure; SD, Standard deviation.

TABLE 2 Reproducibility of the dipper vs non-dipper classification in patients with diabetes

	SBP				DBP				
Dippers	n	%	Agreement (%)	Карра	n	%	Agreement (%)	Карра	
1st recording	32	41			34	52.3			
2nd recording	29	43.9	66.1	0.3	35	53	69.2	0.38	
3rd recording	19	29.2	76.6	0.48	34	52.3	71.8	0.44	
4th recording	19	31.7	54.2	0.02	30	50	57.6	0.15	
Mean	19	26.4	67.6	0.28	37	51.4	66.2	0.32	

Abbreviations: DBP, Diastolic blood pressure; SBP, Systolic blood pressure.

TABLE 3 Reproducibility of the day-to-night percentage change in BP in patients with obesity (BMI > 30)

Nocturnal fall in blood pressure (% of daytime value)	SBP					DBP				
	Mean	Sd	ICC	Correlation	Repeatability	Mean	Sd	ICC	Correlation	Repeatability
1st recording	7.77	7.28	0.324			10.71	8.95	0.339		
2nd recording	6.68	8.31		0.383	55.1	9.34	10.4		0.414	54.5
3rd recording	7.21	7.78		0.326	58.4	10.76	8.43		0.357	57.7
4th recording	6.68	7.28		0.19	64.7	9.53	9.47		0.195	64.9
Mean	6.78	6.38		0.371	57.1	9.8	8.07		0.338	57.3

Abbreviations: BMI, body mass index; DBP, Diastolic blood pressure; ICC, Intraclass correlation coefficient; SBP, Systolic blood pressure; SD, Standard deviation.

TABLE 4 Reproducibility of the dipper vs non-dipper classification in patients with obesity (BMI > 30)

	SBP				DBP	DBP				
Dippers	n	%	Agreement (%)	Карра	n	%	Agreement (%)	Карра		
1st recording	34	41.5			45	54.9				
2nd recording	28	38.4	61.4	0.18	40	54.8	67.1	0.34		
3rd recording	19	27.1	68.7	0.29	37	52.9	68.7	0.37		
4th recording	18	28.6	53.3	-0.045	30	47.6	45	-0.1		
Mean	19	24.1	65.8	0.25	41	51.9	63.2	0.26		

Abbreviations: BMI, Body Mass Index; DBP: Diastolic Blood Pressure; SBP: Systolic Blood Pressure.

1048

TABLE 5 Reproducibility of the day-to-night percentage change in BP in patients with age > 70

Nocturnal fall in blood pressure (% of daytime value)	SBP	SBP					DBP			
	Mean	Sd	ICC	Correlation	Repeatability	Mean	Sd	ICC	Correlation	Repeatability
1st recording	7.76	9.72	0.581			12.48	9.98	0.518		
2nd recording	7.12	9.63		0.58	44.6	12.75	10.15		0.473	50.7
3rd recording	5.69	10.24		0.612	44.3	11.49	10.4		0.499	51
4th recording	6.22	10.29		0.649	42.6	12.17	10.18		0.643	43.3
Mean	5.77	9.11		0.708	38	11.83	8.95		0.607	44.7

Abbreviations: DBP, Diastolic blood pressure; ICC, Intraclass correlation coefficient; SBP, Systolic blood pressure; SD, Standard deviation.

 TABLE 6
 Reproducibility of the dipper vs non-dipper classification in patients with age > 70

	SBP				DBP	DBP			
Dippers	n	%	Agreement (%)	Карра	n	%	Agreement (%)	Карра	
1st recording	39	45.3			53	61.6			
2nd recording	29	37.7	73	0.45	52	67.5	67.6	0.29	
3rd recording	19	26.4	71	0.38	36	50	69.6	0.39	
4th recording	24	36.9	64.5	0.28	38	58.5	77.4	0.53	
Mean	29	33.7	74.7	0.48	48	55.8	69.9	0.38	

Abbreviations: DBP, Diastolic blood pressure; SBP, Systolic blood pressure.

TABLE 7 Reproducibility of the day-to-night percentage change in BP in patients with hypertension: SBP daytime > 135mmHG

Nocturnal fall in blood pressure (% of daytime value)	SBP	SBP					DBP				
	Mean	Sd	ICC	Correlation	Repeatability	Mean	Sd	ICC	Correlation	Repeatability	
1st recording	11.1	9.27	0.562			14.58	11.35	0.604			
2nd recording	7.98	9.12		0.631	40.8	12.1	11.66		0.682	39.1	
3rd recording	9.67	9.97		0.528	48.6	14.4	10.9		0.472	51.3	
4th recording	9.44	10.12		0.631	42.6	14.24	10.69		0.651	42.9	
Mean	8.22	8.7		0.709	38	13	10.11		0.678	39.7	

Abbreviations: DBP, Diastolic blood pressure; ICC, Intraclass correlation coefficient; SBP, Systolic blood pressure; SD, Standard deviation.

TABLE 8 Reproducibility of the dipper vs non-dipper classification in patients with hypertension: SBP > 135mm Hg

SBP					DBP					
Dippers	n	%	Agreement (%)	Карра	n	%	Agreement (%)	Карра		
1st recording	37	57.8			43	67.2				
2nd recording	23	43.4	73.6	0.49	37	69.8	83	0.59		
3rd recording	22	40.7	61.1	0.25	36	66.7	70.4	0.31		
4th recording	21	47.7	61.4	0.24	28	63.6	77.3	0.48		
Mean	21	35.6	69.5	0.42	38	64.4	74.6	0.43		

Abbreviations: DBP, Diastolic blood pressure; SBP, Systolic blood pressure.

1049

Wh fy

TABLE 9 Reproducibility of the day-to-night percentage change in BP using the IDACO criteria

Nocturnal fall in blood pressure (% of daytime value)	SBP					DBP				
	Mean	SD	ICC	Correlation	Repeatability	Mean	SD	ICC	Correlation	Repeatability
1st recording	8.73	8.9	0.512			12.7	9.92	0.483		
2nd recording	7.4	8.7		0.524	48.3	11.6	9.93		0.513	48.9
3rd recording	8.1	9.2		0.503	49.8	12.9	9.57		0.486	50.7
4th recording	7.23	9.82		0.453	52.3	12.1	9.88		0.433	53.4
Mean	7.44	7.96		0.562	46.8	12	8.33		0.536	48.3

Abbreviations: DBP, Diastolic blood pressure; ICC, Intraclass correlation coefficient; SBP, Systolic blood pressure; SD, Standard deviation.

TABLE 10 Reproducibility of the dipper vs non-dipper classification using the IDACO criteria

	SBP				DBP	DBP				
Dippers	n	%	Agreement (%)	Карра	n	%	Agreement (%)	Карра		
1st recording	107	47.8			145	64.7				
2nd recording	81	40.5	65.5	0.3	121	60.5	69	0.34		
3rd recording	75	37.7	68.8	0.37	121	60.8	72.4	0.41		
4th recording	72	38.3	61.2	0.21	111	59	67.6	0.31		
Mean	68	33.3	66.7	0.32	123	60.3	71.1	0.38		

Abbreviations: DBP, Diastolic blood pressure; SBP, Systolic blood pressure.