Letters to the Editor

Consideration of nondipping heart rate during ambulatory blood pressure monitoring to improve cardiovascular risk assessment

La frecuencia cardiaca nondipper *durante la monitorización ambulatoria de la presión arterial mejora la estratificación del riesgo cardiovascular*

To the Editor,

Blood pressure (BP) and heart rate (HR) undergo physiological circadian variations with daytime peaks and night-time troughs. Nondipping, the phenomenon of insufficient day-to-night decline in BP and HR, reflects sympathetic predominance persisting overnight associated with elevated cardiovascular risk. Indeed, nondipping systolic BP is considered a cardiovascular risk factor and is generally determined during ambulatory blood pressure monitoring (ABPM). Nondipping HR has also been shown to predict adverse cardiovascular disease (CVD) prognosis in the general population as well as in hypertension, type 2 diabetes and chronic kidney disease patients, and yet unfortunately it remains overlooked during ABPM.[1]

An impressive study by Hermida et al.[2] on improving CVD risk stratification by using BP-derived parameters from 48-hour ABPM was recently published in *Revista Española de Cardiología*. In the study, 19 949 participants (10 478 men and 9471 women, aged 58.5 ± 14.2 years, without prior CVD events) in the Hygia Project were assessed by 48-hour ABPM and followed up for up to 12.7 years. During the follow-up, 1854 participants experienced a primary CVD event that was defined as per the Framingham study as CVD death, myocardial infarction, coronary revascularization, heart failure, stroke, angina pectoris, or peripheral artery disease. According to the results, substituting BP-derived parameters (asleep systolic BP mean and sleep-time relative systolic BP decline) from 48-hour ABPM for office BP measurement in the Framingham risk score significantly improved calibration, diagnostic accuracy, discrimination, and performance of CVD risk stratification. This highly important study in CVD risk assessment was predominantly based on the Hygia Project, a primary care-based research network established to incorporate ABPM as a routine procedure for cardiovascular risk assessment and diagnosis and management of hypertension.

The authors indicated that they chose asleep systolic BP mean and sleep-time relative systolic BP decline, ie, systolic BP dipping, based on their previous study published in the *European Heart Journal*, in which these were the only BP-derived parameters from 48-hour ABPM that were jointly significant in predicting CVD risk.[3] In fact, in that study, the authors also showed HR-derived parameters (asleep HR mean and sleep-time relative HR decline) from 48-hour ABPM to be associated with adverse CVD outcome. Nonetheless, the significance of HR-derived parameters from ABPM in CVD risk assessment remained unrecognized. Importantly, however, a study by Ben-Dov et al.,[4] including 3957 patients (58% treated for hypertension) assessed by 24-hour ABPM with a mean 7-year follow-up, showed a 34% increase in all-cause mortality per 10% less HR decline at night. In addition, the study compared the effect of nondipping systolic BP and nondipping HR on all-cause mortality prediction. The risk of all-cause mortality was lower among patients with nondipping systolic BP alone, higher in patients with nondipping HR alone, and highest in patients with both nondipping systolic BP and nondipping HR.

Given these results, an opinion is emerging that taking HR-derived parameters (particularly sleep-time relative HR decline, ie, HR dipping), albeit not included in the original Framingham risk score, into account with BP-derived parameters from ABPM and other traditional risk factors would improve CVD risk assessment even further. Moreover, as HR is commonly determined during ABPM, no supplementary measurements are needed. Thus, HR dipping appears to be a readily accessible parameter potentially enabling fine-tuning of CVD risk management, including hypertension pharmacotherapy, at no additional financial burden.

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AUTHORS' CONTRIBUTIONS

T. Baka: concept and writing; A. Domínguez-Rodríguez: critical review; F. Simko: concept and critical review.

CONFLICTS OF INTEREST

None.

Tomas Baka,[a] Alberto Domínguez-Rodríguez,[b,c] and Fedor Simko[a,d,e,*]

[a]*Institute of Pathophysiology, Faculty of Medicine, Comenius University, Bratislava, Slovak Republic*
[b]*Servicio de Cardiología, Hospital Universitario de Canarias, San Cristóbal de La Laguna, Santa Cruz de Tenerife, Spain*
[c]*Departamento de Enfermería, Facultad de Ciencias de la Salud, Universidad de La Laguna, San Cristóbal de La Laguna, Santa Cruz de Tenerife, Spain*
[d]*3rd Department of Internal Medicine, Faculty of Medicine, Comenius University, Bratislava, Slovak Republic*
[e]*Institute of Experimental Endocrinology, Biomedical Research Center, Slovak Academy of Sciences, Bratislava, Slovak Republic*

[*] Corresponding author:
E-mail address: fedor.simko@fmed.uniba.sk (F. Simko).

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Consideration of nondipping heart rate during ambulatory blood pressure monitoring to improve cardiovascular risk assessment. Response

La frecuencia cardiaca nondipper *durante la monitorización ambulatoria de la presión arterial mejora la estratificación del riesgo cardiovascular. Respuesta*

To the Editor,

We appreciate the commentary by Baka et al. Elevated asleep heart rate (HR), and mean and blunted sleep-time relative HR decline (index of HR dipping), both determined by around-the-clock ambulatory blood pressure (BP) monitoring (ABPM), have been identified in several prospective studies as significant prognostic markers of increased cardiovascular disease (CVD) risk. Corroborating and extending these findings, our previously reported evaluation of the data from 18 078 participants in the Hygia Project recruited up to 2015, assessed periodically by 48-hour ABPM, documented the asleep HR mean (per 1-SD elevation, adjusted hazard ratio, 1.16; 95% confidence interval (95%CI), 1.10-1.23; $P < .001$) and the sleep-time relative HR decline (0.81; 95%CI, 0.76-0.86; $P < .001$) were significant markers of CVD outcome, but office HR (1.05; 95%CI, 0.99-0.11; $P = .060$) and awake ambulatory HR mean (1.03; 95%CI, 0.97-1.09; $P = .318$) were not.[1] Furthermore, results of the time-dependent Cox regression analysis documented that the increase during follow-up in sleep-time relative HR decline toward a more normal dipper HR pattern was significantly associated with reduced CVD risk (0.90; 95%CI, 0.81-0.99; $P = .032$).[1]

We used an extended database with 19 949 participants in the Hygia Project without previous CVD events to document the marked limitations of current CVD risk stratification models, including the CVD Framingham risk score, based exclusively on office BP.[2] In so doing, we replaced office BP by the stronger ABPM-derived prognostic markers of CVD risk, namely asleep systolic BP mean and sleep-time relative systolic BP decline, but kept for proper comparison all other variables—age, sex, smoking, total and HDL-cholesterol, hypertension treatment, and diabetes—of the original Framingham scale. The resulting CVD stratification model showed significantly improved calibration, diagnostic accuracy, discrimination, and performance (always $P < .001$), but it is not a completely optimal or representative approach for ABPM-based CVD risk assessment. Beyond sleep-time relative HR decline (0.87 [0.83-0.92]; $P < .001$), other highly significant confounding variables, including chronic kidney disease, glomerular filtration rate, and fasting glucose, must also be incorporated into a more accurate CVD stratification model. Further investigation on how the sleep-time relative HR decline can be efficiently increased by therapy is warranted.

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AUTHORS' CONTRIBUTIONS

All authors have contributed equally in composing this response letter.

CONFLICTS OF INTEREST

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Ramón C. Hermida,[a,*] Artemio Mojón,[a] Michael H. Smolensky,[b,c] and José R. Fernández[a]

[a]*Laboratorio de Bioingeniería y Cronobiología, Atlantic Research Center for Information and Communication Technologies (atlanTTic), Universidad de Vigo, Pontevedra, Spain*
[b]*Department of Biomedical Engineering, Cockrell School of Engineering, The University of Texas at Austin, Austin, Texas, United States*
[c]*Department of Internal Medicine, McGovern School of Medicine, The University of Texas Health Science Center at Houston, Houston, Texas, United States*

[*] Corresponding author:
E-mail address: rhermida@uvigo.es (R.C. Hermida).

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