ESC
European Society
of Cardiology

DISCUSSION FORUM

Asleep (not night-time) blood pressure as prognostic marker of cardiovascular risk

Ramón C. Hermida[1]*, Juan J. Crespo[1,2], Alfonso Otero[3], Manuel Domínguez-Sardiña[2], Ana Moyá[4], María T. Ríos[1,2], María C. Castiñeira[1,5], Pedro A. Callejas[1,2], Lorenzo Pousa[1,2], Elvira Sineiro[1,4], José L. Salgado[1,2], Carmen Durán[2], Juan J. Sánchez[1,6], José R. Fernández[1], Artemio Mojón[1], and Diana E. Ayala[1]

[1]Bioengineering & Chronobiology Laboratories, Atlantic Research Center for Information and Communication Technologies (AtlantTIC); University of Vigo, Vigo, Spain; [2]Estructura de Gestión Integrada de Vigo, Servicio Galego de Saúde (SERGAS), Vigo, Spain; [3]Servicio de Nefrología, Complejo Hospitalario Universitario, Estructura de Gestión Integrada de Ourense, Verín y O Barco de Valdeorras, Servicio Galego de Saúde (SERGAS), Ourense, Spain; [4]Estructura de Xerencia Integrada Pontevedra e O Salnés, Servicio Galego de Saúde (SERGAS), Pontevedra, Spain; [5]Estructura de Gestión Integrada de Lugo, Cervo y Monforte de Lemos, Servicio Galego de Saúde (SERGAS), Lugo, Spain; and [6]Estructura de Gestión Integrada de Santiago de Compostela, Servicio Galego de Saúde (SERGAS), Santiago de Compostela, Spain

This commentary refers to 'Asleep blood pressure: significant prognostic marker of vascular risk and therapeutic target for prevention', by R.C. Hermida et al., 39:4159–4171.

The commentary by Torp-Pedersen et al., challenging our conclusion concerning the prognostic merit of asleep blood pressure (BP) as the most relevant BP-derived marker of cardiovascular disease (CVD) risk,[1] contains several arguable statements:

(1) We *not only* conducted Cox-survival but also discriminative/predictive analyses of BP parameters by C-statistic and Akaike Information Criterion methods. Results document asleep systolic BP (SBP) mean provide significantly better CVD-outcome prediction than office SBP and that adding office or awake SBP to the model already including asleep SBP mean fails to improve prediction.[1]

(2) The argument by Top-Pedersen et al. for exclusive use of the C-statistic for model selection is not supported by Hlatky et al.,[2] who specifically state: 'The C-index does not test whether the risk predictions are accurate or whether the risk model is well calibrated. . . is relatively insensitive to change, and may not increase appreciably even when a new marker is statistically significant and independently associated with risk'.

(3) The C-statistic, frequently used in *diagnostic* testing, is suboptimal for assessing models that *predict* risk.[1–3] As an illustrative example of Cook's impecable contentions,[3] the C-statistic for the model including all significant confounders documented in our study[1] plus asleep SBP mean and sleep-time relative SBP decline is 0.812 95%CI (0.801–0.823). Removing diabetes or sex yields C-statistics of 0.812 (0.800–0.823) and 0.807 (0.795–0.819), respectively, mistakenly suggesting neither diabetes nor sex is

'predictive' of CVD-outcome despite their well-recognized relevance as CVD risk markers.

(4) Torp-Pedersen et al. do not seem to properly describe our findings by refering to an external environmental marker, i.e., 'night-time' BP rather than the internal biological marker of 'sleep-time' BP that is our specific focus. Endogenous circadian rhythms in neuroendocrine, endothelial, vasoactive peptide, opioid, and haemodynamic parameters—including renin, angiotensin, and aldosterone—that are mechanisms of the circadian BP variation are all synchronized by the rest/activity, not the day/night, cycle. As already discussed,[1] reliance on arbitrary and fixed clock-hours not fully representative of the individualized rest/activity pattern to calculate 'daytime/night-time' BP means plus exclusive dependence on the C-statistic might be among the potential limitations of the reported findings by Torp-Pedersen et al.

Conflict of interest: none declared.

References

1. Hermida RC, Crespo JJ, Otero A, Domínguez-Sardiña M, Moyá A, Ríos MT, Castiñeira MC, Callejas PA, Pousa L, Sineiro E, Salgado JL, Durán C, Sánchez JJ, Fernández JR, Mojón A, Ayala DE; for the Hygia Project Investigators. Asleep blood pressure: significant prognostic marker of vascular risk and therapeutic target for prevention. *Eur Heart J* 2018;**39**:4159–4171.
2. Hlatky MA, Greenland P, Arnett DK, Ballantyne CM, Criqui MH, Elkind MSV, Go AS, Harrell FE, Hong Y, Howard BV, Howard VJ, Hsue PY, Kramer CM, McConnell JP, Normand S-LT, O'Donnell CJ, Smith SC, Wilson PWF; on behalf of the American Heart Association Expert Panel on Subclinical Atherosclerotic Diseases and Emerging Risk Factors and the Stroke Council. Criteria for evaluation of novel markers of cardiovascular risk: a scientific statement from the American Heart Association. *Circulation* 2009;**119**:2408–2416.
3. Cook NR. Use and misuse of the receiver operating characteristic curve in risk prediction. *Circulation* 2007;**115**:928–935.

---

* Corresponding author. Tel: 34-986-812148, Fax: 34-986-812116, Email: rhermida@uvigo.es

A complete list of the members of the Hygia Project is provided elsewhere.[1]