

Seasonal Blood Pressure Variation: A Neglected Confounder in Clinical Hypertension Research and Practice

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For more than a century blood pressure (BP) measured by the doctor in the office has been recognized as an indisputable predictor of cardiovascular morbidity and mortality.^{1,2} However, BP is known to show dynamic variability in response to the physical and emotional challenges of routine daily activities, which may confound any investigation involving BP changes.³

Many factors are known to influence BP readings,¹ including the physical and emotional challenges of routine daily activities, the setting (office, home, work), the observer (doctor, nurse, self-measurement, automated unattended), the device (auscultatory, automated), the patient's posture (seated, standing, lying), the time of measurement (morning, evening, nighttime sleep), the measurement schedule (number of readings and those averaged), talking, exercise, meals, smoking, coffee, alcohol, and time of antihypertensive drug intake. In recognizing these confounding factors, international recommendations have standardized the methodologies for BP evaluation in the office and out-of-the-office to minimize their influence and improve the accuracy of BP evaluation.^{4,5}

In the *American Journal of Hypertension* Gepts *et al.*⁶ have added to this list of confounders by demonstrating how seasonal variations in BP can influence the interpretation of interventions aiming at improving BP control. In this study, when seasonality was not accounted for, a significant negative association of the

study intervention on BP control was observed. However, when BP seasonality was taken into account, they showed that the intervention had no effect on BP control.

It is surprising that this major confounder has been systematically ignored for so long. A recent review and meta-analysis of 47 published trials which examined seasonal changes in BP⁷ showed that the seasonal BP variation is a global phenomenon affecting all age groups, both sexes, and normotensive and hypertensive subjects. Meta-analysis of these trials showed an average seasonal BP decline in the high-temperature season of 6/3 mm Hg (systolic/diastolic) for office and home BP and 3.5/2 mm Hg for daytime ambulatory BP, and a small rise in nighttime ambulatory BP (1.3/0.5 mm Hg).⁷ Importantly, these changes were greater in treated hypertensive patients and in older individuals.⁷ Thus, these findings suggest that the magnitude of the seasonal BP change is comparable to the reduction that might be expected from an effective antihypertensive drug, particularly in elderly patients.

The 2017 American College of Cardiology/American Heart Association² as well as the 2018 European Society of Cardiology/European Society of Hypertension guidelines¹ for hypertension do not mention the seasonal BP variation phenomenon, and no recommendations are provided for guiding the practicing physicians on its potential implications in treating hypertension.

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Table 1. Consequences of not adjusting the results of clinical hypertension trials for the seasonal BP variation

- Overestimation of the long-term BP variability
- Underestimation of the long-term reproducibility of methods for measuring BP
- Underestimation of the BP lowering effects of drugs (or overestimation depending on the direction of ambient temperature change)
- Confounding of the association of elevated BP with cardiovascular event risk
- Confounding of the effect of drugs and other interventions on cardiovascular event risk

Abbreviation: BP, blood pressure.

The European Society of Hypertension Working Group on BP Monitoring and Cardiovascular Variability recently published a consensus statement on the seasonal variation in BP,⁸ in which the evidence on the epidemiology, pathophysiology, relevance, and magnitude of the seasonal BP variation was presented together with recommendations for practicing physicians.⁸ The potential impact of the seasonal BP variation on the interpretation of clinical hypertension research was also discussed,⁸ leading to the conclusion that failure to take this factor into account may have distorted the findings of numerous published clinical hypertension trials and epidemiological surveys (Table 1).

In conclusion, the article by Gepts *et al.*⁶ clearly demonstrated that the environmental temperature must be taken into account in clinical hypertension research when evaluating or comparing BP measurements taken on different occasions throughout different seasons. Clinical trials using office or out-of-office BP measurements as efficacy measures, which last long enough to be influenced by ambient temperature change, need to be adjusted for the seasonal variation in BP. Such an adjustment should be proportional to the change in environmental temperature and should be based on BP changes observed at the same time interval without intervention and assessed using the same BP measurement methodology.

DISCLOSURE

The authors declared no conflict of interest.

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